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1 **Magnitude and direction of parasite-induced phenotypic**
2 **alterations: a meta-analysis in acanthocephalans**

3
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16
17 **ABSTRACT**

18 Several parasite species have the ability to modify their host's phenotype to their own
19 advantage thereby increasing the probability of transmission from one host to another. This
20 phenomenon of host manipulation is interpreted as the expression of a parasite extended
21 phenotype. Manipulative parasites generally affect multiple phenotypic traits in their hosts,
22 although both the extent and adaptive significance of such multidimensionality in host
23 manipulation is still poorly documented. To review the multidimensionality and magnitude of
24 host manipulation, and to understand the causes of variation in trait value alteration, we

25 performed a phylogenetically corrected meta-analysis, focusing on a model taxon:
26 acanthocephalan parasites. Acanthocephala is a phylum of helminth parasites that use
27 vertebrates as final hosts and invertebrates as intermediate hosts, and is one of the few
28 parasite groups for which manipulation is predicted to be ancestral. We compiled 279
29 estimates of parasite-induced alterations in phenotypic trait value, from 81 studies and 13
30 acanthocephalan species, allocating a sign to effect size estimates according to the direction of
31 alteration favouring parasite transmission, and grouped traits by category. Phylogenetic inertia
32 accounted for a low proportion of variation in effect sizes. The overall average alteration of
33 trait value was moderate and positive when considering the expected effect of alterations on
34 trophic transmission success (signed effect sizes, after the onset of parasite infectivity to the
35 final host). Variation in the alteration of trait value was affected by the category of phenotypic
36 trait, with the largest alterations being reversed taxis/phobia and responses to stimuli, and
37 increased vulnerability to predation, changes to reproductive traits (behavioural or
38 physiological castration) and immunosuppression. Parasite transmission would thereby be
39 facilitated mainly by changing mainly the choice of micro-habitat and the anti-predation
40 behaviour of infected hosts, and by promoting energy-saving strategies in the host. In
41 addition, infection with larval stages not yet infective to definitive hosts (acanthella) tends to
42 induce opposite effects of comparable magnitude to infection with the infective stage
43 (cystacanth), although this result should be considered with caution due to the low number of
44 estimates with acanthella. This analysis raises important issues that should be considered in
45 future studies investigating the adaptive significance of host manipulation, not only in
46 acanthocephalans but also in other taxa. Specifically, the contribution of phenotypic traits to
47 parasite transmission and the range of taxonomic diversity covered deserve thorough
48 attention. In addition, the relationship between behaviour and immunity across parasite
49 developmental stages and host–parasite systems (the neuropsychimmune hypothesis of host

50 manipulation), still awaits experimental evidence. Most of these issues apply more broadly to
51 reported cases of host manipulation by other groups of parasites.

52

53 *Key words:* behaviour, helminth; host–parasite interaction, manipulation, multidimensionality,
54 phylogenetic meta-analysis, publication bias, ribosomal DNA, trophic transmission.

55

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87 **I. INTRODUCTION**

88 Several parasites bring about phenotypic alterations in their hosts that appear to increase their
89 own fitness at the expense of that of their hosts (Poulin, 1995; Moore, 2002; Thomas, Adamo
90 & Moore, 2005; Cézilly *et al.*, 2010). Such parasite-induced phenotypic alterations (PIPAs)
91 can take different forms, through affecting, for instance, the physiology (Plastow, Troussard
92 & Cézilly, 2001; Tain, Perrot-Minnot & Cezilly, 2006; Perrot-Minnot & Cezilly, 2013; Guler
93 *et al.*, 2015; Kopp *et al.*, 2016; Perrot-Minnot, Maddaleno & Cézilly, 2016), reproduction
94 (Bollache, Gambade & Cézilly, 2001; Bollache, Rigaud & Cézilly, 2002; Rauque & Semenas,
95 2009; Bollache, 2016) or appearance (Lewis, 1977; Camp & Huizinga, 1979; Oetinger &
96 Nickol, 1981; Amato *et al.*, 2003; Wesółowska & Wesółowski, 2014) of infected hosts.
97 However, most studies of PIPA concern the altered behaviour of host species. For instance,
98 several species of ectoparasitoid wasps are known to modify the web-building behaviour of
99 their spider hosts (Eberhard, 2000; Matsumoto, 2008; Korenko *et al.*, 2014; Takasuka *et al.*,

100 2015; Kloss *et al.*, 2017). Just before the wasp enters its final stage of development, the spider
101 host builds a modified web in the form of a ‘cocoon’ (Eberhard, 2000) that appears to
102 enhance the survival of the parasitoid pupae. Both rodents and chimpanzees infected with
103 *Toxoplasma gondii* famously lose their innate aversion to the urine of feline predators
104 (Berdoy, Webster & McDonald, 2000; Dass & Vyas, 2014; Poirotte *et al.*, 2016), a
105 phenomenon that presumably increases the transmission of the parasite to its final host.
106 Similarly, several species of helminths with complex life cycles are known to alter the anti-
107 predation behaviour of their intermediate arthropod hosts in ways that appear to enhance
108 trophic transmission to final hosts (Hechtel, Johnson & Juliano, 1993; Kaldonski, Perrot-
109 Minnot & Cézilly, 2007; Sánchez, Georgiev & Green, 2007). For instance, whereas
110 uninfected crustacean amphipods are significantly repulsed by the chemical cues originating
111 from a fish predator, infected ones are significantly attracted to the odour (Baldauf *et al.*,
112 2007; Perrot-Minnot, Kaldonski & Cézilly, 2007). Most of the time, such phenotypic
113 alterations are interpreted as expressions of the extended phenotype (*sensu* Dawkins, 1982) of
114 the parasite species, whose ability to ‘manipulate’ its host has evolved by natural selection
115 (Moore, 2002; Thomas *et al.*, 2005; Hughes, Brodeur & Thomas, 2012). Alternatively, they
116 could correspond to simple pathological effects (Chow & Mackauer, 1999; Edelaar, Drent &
117 De Goeij, 2003; Schutgens *et al.*, 2015) or to an adaptive host response (Smith Trail, 1980;
118 Poulin, 1992; Poulin, Brodeur & Moore, 1994). Whether the magnitude of parasite
119 phenotypic alterations varies in relation to its consequences for the parasite and its host is
120 poorly documented.

121 Although adaptive host manipulation has become a sort of paradigm in evolutionary
122 parasitology and behavioural ecology (Poulin, 2000; Moore, 2002; Thomas *et al.*, 2005;
123 Bakker, Frommen & Thuenken, 2017), growing evidence suggests that the ‘purposive design’
124 (*sensu* Poulin, 1995) of phenotypic alterations induced by parasites should be examined with

125 more caution. A crucial step in validating the manipulation hypothesis is to show
126 convincingly that a direct *causal* relationship exists between altered host phenotype and
127 enhanced completion of the life cycle (Cézilly *et al.*, 2010). Indeed, behavioural alterations
128 observed in infected hosts that *seemingly* enhance the completion of the parasite's life cycle
129 may not *actually* contribute to it. For instance, the behavioural alterations displayed by
130 tenebrionid beetles infected with *Hymenolepis diminuta*, including reduced activity,
131 concealment and photophobia (Hurd & Fogo, 1991; Robb & Reid, 1996), were initially
132 interpreted as a case of manipulation. However, such phenotypic alterations do not necessarily
133 result in a differential vulnerability of infected and uninfected beetles to predation by rodent
134 final hosts (Webster *et al.*, 2000). Similar conclusions have been drawn from recent studies of
135 two historical models of host manipulation. Crustacean amphipods serve as intermediate hosts
136 for various acanthocephalan parasites that use different species of vertebrates as final hosts.
137 Inside their intermediate hosts, larval acanthocephalans progressively develop into
138 cystacanths, the infective stage for the definitive host. Cystacanths of several acanthocephalan
139 species have a carotenoid-based, bright orange colouration (Gaillard *et al.*, 2004) that can be
140 seen through the translucent cuticle of their hosts, such that infected hosts are particularly
141 conspicuous, at least to the human eye. In addition, gammarids infected with
142 acanthocephalans show altered behaviour, including reduced photophobia. Bethel & Holmes
143 (1973, 1977) were the first to provide evidence for a causal link between the altered behaviour
144 of gammarids infected with larval acanthocephalans and their increased vulnerability to
145 predation, and the phenomenon was quickly regarded as a compelling example of host
146 manipulation (Dawkins, 1982). Bakker, Mazzi & Zala (1997) went further by arguing that
147 both the modified appearance and the altered phototactic behaviour of *Pomphorhynchus*
148 *laevis*-infected *Gammarus pulex* were responsible for their increased vulnerability to
149 predation by three-spined sticklebacks, *Gasterosteus aculeatus*. However, more recent

150 investigations using phenotypic engineering to manipulate one trait at a time (Kaldonski *et*
151 *al.*, 2009; Perrot-Minnot *et al.*, 2012) demonstrated convincingly that neither parasite's colour
152 nor the altered phototactic behaviour of infected hosts *alone* contribute to the increased
153 vulnerability of *P. laevis*-infected gammarids to fish predation. Therefore, several phenotypic
154 changes might act synergistically to enhance trophic transmission.

155 Similarly, Worth, Lymbery & Thompson (2013) questioned the adaptiveness of
156 behavioural alterations induced by *T. gondii* in rodents, based on several lines of evidence.
157 First, studies of mice and rats have resulted in conflicting results about what behaviours are or
158 are not affected by infection. Second, behavioural alterations similar to those coincidental
159 with *T. gondii* infection can also be induced by *Eimeria vermiformis*, a parasite that does not
160 rely on trophic transmission to complete its life cycle [Kavaliers & Colwell, 1995; see also
161 Cator *et al.* (2013) for a related result in a markedly different host–parasite association].
162 Third, there is, surprisingly enough, no direct evidence that rodents infected with *T. gondii* are
163 more vulnerable to predation by cats. Fourth, even if such evidence was available, it appears
164 that cats and sexual reproduction might not be crucial for the survival, transmission, and
165 maintenance of *T. gondii* in a population (Worth *et al.*, 2013). The overall evidence thus
166 suggests that the apparent ‘purposive design’ of parasite-induced phenotypic alterations does
167 not guarantee a causal relationship between manipulation and enhanced trophic transmission.
168 More to the point, it is still unclear to what extent the consequences of host manipulation, in
169 terms of enhanced completion of the parasite's life cycle, depends on its magnitude.

170 In addition, although most studies have considered a single phenotypic alteration at a
171 time, it is increasingly acknowledged that, most often, manipulative parasites affect more than
172 one phenotypic dimension in their hosts (Gotelli & Moore, 1992; Cézilly & Perrot-Minnot,
173 2005; Cézilly, Favrat & Perrot-Minnot, 2013). Such multidimensionality might be adaptive if,
174 for instance, it allows the parasite to enhance the completion of its life cycle under a large

175 range of ecological circumstances (Thomas, Poulin & Brodeur, 2010). Under this scenario,
176 multidimensionality may have arisen from the progressive addition of several phenotypic
177 dimensions that are manipulated independently of each other through distinct physiological
178 pathways. Alternatively, multidimensionality in manipulation may stem from the major
179 disruption of some specific physiological mechanism, with cascading effects affecting various
180 phenotypic dimensions (Cézilly & Perrot-Minnot, 2010). For instance, crustacean amphipods
181 infected with fish acanthocephalans show a variety of modified phenotypic traits (Cézilly *et*
182 *al.*, 2013), including an increased serotonergic activity in the brain (Tain *et al.*, 2006).
183 Interestingly, multidimensionality in manipulation as observed in *G. pulex* infected with *P.*
184 *laevis* can be partly mimicked in uninfected individuals by the injection of serotonin (Perrot-
185 Minnot, Sanchez-Thirion & Cézilly, 2014), thus providing support for the second hypothesis.
186 To what extent this finding applies to other cases of multidimensionality in manipulation
187 remains an open question. In addition, whether the existence of a single mechanism would
188 result in co-variation among individuals in the magnitude of the various phenotypic
189 alterations simultaneously brought about by a parasite species remains unclear (see Bailly,
190 Cézilly & Rigaud, 2018).

191 The interest in manipulative parasites is however not limited to their value as a
192 supposedly perfect example of an extended phenotype. Growing attention has been given to
193 the role that such parasites play in ecosystems through their influence on the behaviour and
194 trophic niches of their hosts and, ultimately, on trophic cascades (Thomas *et al.*, 1997;
195 Thomas *et al.*, 1998; Lefèvre *et al.*, 2009; Lafferty & Kuris, 2012; Sato *et al.*, 2012; Boze &
196 Moore, 2014; Britton & Andreou, 2016; Reisinger & Lodge, 2016). Still, the precise impact
197 of manipulative parasites on ecosystem dynamics remains unclear, partly because the
198 relationship between the magnitude of phenotypic alterations and their ecological
199 consequences is difficult to assess. More to the point, the ability of parasites to manipulate

200 their hosts might be modulated by various environmental variables. For instance, temperature
201 recently has been shown to affect the extent of manipulation of phototaxis in amphipods
202 infected by acanthocephalans, but not that of geotaxis or refuge use (Labaude, Cézilly &
203 Rigaud, 2017a). Environmental influences and infection with manipulative parasites may thus
204 have interactive or additive effects on the phenotype of infected hosts (see Labaude, Rigaud &
205 Cézilly, 2017b) and, therefore contribute directly to the observed variation in the magnitude
206 of manipulation within and among host–parasite associations, with potential consequences at
207 the level of ecosystems.

208 Whether host manipulation is studied from the point of view of its evolutionary routes
209 (Thomas, Rigaud & Brodeur, 2012), its underlying mechanisms (Perrot-Minnot & Cézilly,
210 2013) or its ecological consequences (Lafferty & Kuris, 2012; Labaude, Rigaud & Cézilly,
211 2015b), an important question is what causes variation at different levels in the magnitude of
212 phenotypic alterations coincidental with infection by manipulative parasites. Variation in the
213 extent of such phenotypic alterations exists both within and among infected individuals in a
214 single host population, as well as among host populations (Thomas *et al.*, 2011; Fayard,
215 Cézilly & Perrot-Minnot, 2019) or among host species infected with the same parasite
216 (Gotelli & Moore, 1992; Bauer *et al.*, 2000; Tain, Perrot-Minnot & Cézilly, 2007). The
217 relative importance of host and parasite phylogenies, the type of altered trait or the
218 consequences in terms of enhanced completion of the parasite’s life cycle remain however
219 poorly documented, although a few attempts have been made to provide quantitative reviews
220 of the existing literature on host manipulation (Moore & Gotelli, 1990; Poulin, 1994, 2000;
221 McElroy & de Buron, 2014; Nakagawa *et al.* 2015). In the latter approach, meta-analysis
222 constitutes a valuable tool (Poulin & Forbes, 2012), particularly to quantify the heterogeneity
223 observed in the magnitude of host manipulation. So far, however, meta-analysis has seldom
224 been used for that purpose. Using a meta-analytic framework, Poulin (1994, 2000) and

225 Nakagawa *et al.* (2015) provided valuable insights on the influence of parasite taxa and
226 behavioural traits on the magnitude of the effect of parasites on their hosts. Interestingly,
227 based on 137 comparisons between the behaviour of infected and uninfected hosts, Poulin
228 (2000) found that the reported values of effect size indicating host manipulation tended to
229 decrease over time. He further suggested that this may be due to the fact that most of the
230 earlier investigations of host manipulation concerned acanthocephalan parasites, in which the
231 ability to manipulate host phenotype is regarded as an ancestral, well-established character
232 (Moore, 1984), whereas, later on, evidence for manipulation was sought in a larger range of
233 host–parasite associations (Poulin, 2000). The same, although non-significant, trend for effect
234 size becoming smaller over time was reported in an updated analysis based on 202 effect sizes
235 (Nakagawa *et al.*, 2015). As acanthocephalans tend to have marked effects on their hosts
236 (Bakker *et al.*, 2017), it might have been difficult to obtain similar results in other parasites
237 with a relatively smaller ability to manipulate their hosts (Nakagawa *et al.*, 2015). Another
238 recent analysis, focusing on host performance (defined as a physical quantity that measures
239 how well an organism can execute a given behaviour or task) and considering the literature
240 published until 2013, failed to detect the same effect, but found some evidence for an increase
241 in the magnitude of the effect of parasites on their hosts with publication year (McElroy & de
242 Buron, 2014). However, the final data set in that study was based on only 49 studies.

243 The use of meta-analysis to analyse both the direction and magnitude of parasite-
244 induced phenotypic alterations introduces several difficulties. First, not all published articles
245 provide enough statistical information to allow the computation of effect sizes, such that final
246 data sets available for meta-analysis might be of reduced size, thus increasing the risk of type
247 II error (Arnqvist & Wooster, 1995). Second, there exists an unequal representation of the
248 various species of hosts and parasites in the scientific literature on host manipulation, and this
249 taxonomic bias is likely to result in non-random data sets (Lajeunesse, 2010). This is why it is

250 highly recommended to incorporate phylogenetic information in ecological meta-analyses
251 (Chamberlain *et al.*, 2012).

252 Here, we provide a meta-analysis of the existing literature about the phenotypic
253 alterations induced by acanthocephalan parasites in their intermediate hosts. Although around
254 1300 species of acanthocephalan parasites have been described, their phylogenetic
255 relationships within Metazoa remain controversial (García-Varela & León, 2015). Based on
256 morphological, ecological and molecular evidence, acanthocephalan parasites have been
257 divided into four classes: Archiacanthocephala, corresponding to the most basal clade, and
258 Palaeacanthocephala, Eoacanthocephala, and Polyacanthocephala, corresponding to three
259 derived clades (Amin, 1987; Kennedy, 2006; García-Varela & León, 2015). Although the
260 evolution of acanthocephalans is characterized by a multiplicity of host-switching events
261 (García-Varela & León, 2015), they tend to have strong and diversified effects on the
262 phenotype of their hosts (Cézilly *et al.*, 2013; Bakker *et al.*, 2017). Palaeacanthocephalans
263 represent the most diverse and best-studied class of acanthocephalans, while published studies
264 of host manipulation in other acanthocephalan groups are scarce (see Section II).

265 We reviewed phenotypic alterations induced by acanthocephalan parasites by
266 considering two features: (i) the alteration of mean trait value, measured as the increase or
267 decrease in a host phenotypic trait value expected to increase parasitic transmission in
268 infected hosts; (ii) the magnitude of alterations, quantifying the influence of the parasite on
269 the host's phenotype irrespective of its consequence on parasite transmission. For the former,
270 we used signed effect sizes measured at the last developmental stage infective to the final host
271 (cystacanth). For the latter, we also included effect size estimates from larval stages not yet
272 infective to final hosts (acanthella). We first examined the extent to which the alteration of
273 mean trait value and the magnitude of alteration was affected by phylogeny. We then
274 quantified the effects of acanthocephalans on their host phenotype to answer three questions:

275 (1) how strong is the overall effect of infection? (2) Following the parasite manipulation
276 hypothesis, are these alterations of host trait value likely to enhance parasite transmission on
277 average? (3) How variable is alteration of the trait value according to several factors including
278 trait categories (multidimensionality) and publication year?

279

280 **II. METHODS**

281 **(1) Literature search**

282 Studies on acanthocephalan-induced phenotypic alterations were searched in the the *Web of*
283 *Science* and *Google Scholar* databases by using combinations of “acanthocephala*” and
284 “behav*” or “physio*” or “morpho*” or “size” or “chang*” or “host” or “predat*” or
285 “reproduct*” or “survival” or “mortality” key words. The search included studies published
286 until January 2018. From 3531 studies, and after sequential removals because of lack of
287 sufficient quantitative information, we obtained a database of 81 studies (PRISMA flow
288 diagram, Fig. 1). All studies included in analyses are identified with an asterisk in the
289 reference list.

290

291 **(2) Data collection**

292 For each study, we recorded the year of publication, parasite taxonomy (from the class to the
293 species) and stage (non-infective acanthella or infective cystacanth), intermediate host
294 taxonomy (class and species), phenotypic traits measured and the magnitude of alteration
295 associated with infection (effect size), sample size (infected and uninfected individuals) and
296 infection type (natural or experimental). Following the recommendations of Noble *et al.*
297 (2017), we sought for sources of non-independence stemming from within-study design, in
298 addition to phylogeny-, species- and study-level non-independence. We identified two sources
299 of within-study covariance: effect sizes estimated for different parasite species using the same

300 controls ('shared treatment comparison' or 'shared controls'), and effect sizes measured on
301 the same individual ('shared traits') (Noble *et al.*, 2017).

302

303 **(3) Categorization of host phenotypic traits**

304 We categorized host phenotypic traits into five groups: 'behaviour', 'life history',
305 'morphology' and 'physiology' according to Mousseau & Roff (1987), and vulnerability to
306 'predation' (Table 1). We further subdivided each category into trait subcategories: for
307 behaviour, 'activity', 'protection', 'response to stimuli' and 'taxis/phobia'; for life history,
308 'body condition', 'foraging', 'intraspecific interaction', 'reproduction' and 'survival'; for
309 morphology, 'growth' and 'colour'. We subdivided the category physiology into 'immunity',
310 'energy reserves/metabolism', and 'neurophysiology'. Finally, within the trait category
311 predation, we differentiated two types of predators, 'non-host' and 'suitable host'.

312

313 **(4) Calculation of effect sizes**

314 Following the recommendation of Nakagawa *et al.* (2017) for comparisons between two
315 treatments (here, parasite infection and control), we used standardized effect sizes based on
316 means and standard deviations, mostly with Cohens d (Cohen, 1988). In some cases, we also
317 extracted this information from figures with the 'digitize' R package (Poisot *et al.*, 2016).
318 When means and standard deviations were not available in the publication, we attempted to
319 contact the authors directly. When proportions of individuals were given, we used the Odds
320 ratio (Borenstein *et al.*, 2009). As not all studies reported the same effect size metrics, their
321 direct comparison was not possible. We used conversions from Borenstein *et al.* (2009) to
322 obtain a common metric of effect size, the correlation coefficient r , allowing comparison
323 between studies. To conduct the analyses, we then converted each r into a Fisher Zr using the
324 Fisher r to Z transformation (Borenstein *et al.*, 2009), with $Zr = 0.5 \times \ln((1 + r)/(1 - r))$. After

325 the analyses, meta-analytic Zr means were back-transformed into meta-analytic r means.
326 Values of 0.1, 0.3 and 0.5 were interpreted as low, moderate and strong effects, respectively
327 (Cohen, 1988).

328

329 **(5) Signed effect sizes according to parasite transmission**

330 We assigned a sign to each effect size according to the direction of alteration, whether an
331 increase or a decrease in mean trait value, that was expected to enhance trophic transmission.
332 Positive values of effect sizes were associated with alterations in a host trait expected to
333 enhance parasite transmission by increasing encounter rate between infected prey and
334 predators (ERH: encounter rate hypothesis) (Table 1). When the effect of PIPA on parasite
335 transmission did not directly affect encounter rate, positive values were assigned to alterations
336 that would favour host survival independently of predation, for instance by decreasing host
337 energetic expenditure (ESH: energy-saving hypothesis) (Table 1). The rationale is that
338 parasite transmission relies on host survival until predation, in part modulated by energy
339 reserves invested in host maintenance (traded-off against other functions) and parasite growth.
340 Therefore, the fitness of trophically transmitted parasites relies partly on the survival of
341 intermediate hosts until predation. In some cases, the direction of alteration for optimal
342 parasite transmission was ambiguous, as either an increase or a decrease in the expression of
343 one trait could contribute to increased parasite transmission (Table 1). We therefore ran
344 alternative analyses without these ambiguous traits, following Cally, Stuart-Fox & Holman
345 (2019), and present these additional results as online Supporting Information.

346

347 **(6) Choice of moderators**

348 Five factors were considered as fixed effects.

349

350 (a) *Category of traits*

351 As parasite transmission depends critically on prey–predator interactions, the behaviour of
352 infected intermediate hosts is of prime importance relative to other phenotypic traits. In
353 addition, behavioural traits are more plastic than, for instance, morphological traits (Price,
354 Qvarnström & Irwin, 2003). One may therefore expect behavioural traits to be more easily
355 altered by ‘manipulative’ parasites than morphological traits, resulting in differences in effect
356 size between behavioural and morphological traits.

357

358 (b) *Infection type and environmental conditions*

359 One criticism of experimental studies on host manipulation by parasites is that laboratory
360 conditions imperfectly reflect natural ones. Experimental infection procedure and
361 maintenance conditions (light intensity, temperature, host density, stress of handling and
362 maintenance) could impact the expression of phenotypic traits, and thus affect the estimates of
363 effect size.

364

365 (c) *Parasite developmental stage*

366 Two different phenomena with opposite effects could alter the vulnerability to predation and
367 survival probability of infected intermediate hosts (Parker *et al.*, 2009). ‘Predation
368 suppression’ is used to refer to manipulations by immature parasites that decrease the
369 vulnerability to predation of their intermediate host. Conversely, ‘predation enhancement’ is
370 used to refer to manipulations that increase vulnerability to predation of the intermediate host
371 at a developmental stage at which the parasite is infective to its final host. In
372 acanthocephalans, acanthella are developmental stages at which the parasite is unable to
373 establish in an appropriate final host, while the cystacanth is the last developmental stage in
374 the intermediate host and is infective to final host. Dianne *et al.* (2011) found experimental

375 evidence for both effects in *G. pulex* infected with *P. laevis*. Although opposite effects
376 between acanthella and cystacanth infections have been reported several times, it is not clear
377 whether they are of the same magnitude.

378

379 *(d) Publication year*

380 Host manipulation by parasites has been actively investigated in the field of host–parasite
381 interactions since the study of Holmes (1972) pointed out the adaptive value of manipulation.
382 Several criticisms of this hypothesis and alternative explanations emerged almost 20 years
383 later from the review of Moore & Gotelli (1990). The approach used to study a phenomenon
384 can change according to current paradigms, and this may lead to different conclusions
385 (Poulin, 2000). As a consequence of growing interest in the topic, and methodological and
386 technical progress, it is possible that trends in magnitude of acanthocephalan-induced
387 alterations reported in the literature could appear through time.

388

389 *(e) Sample size*

390 Confidence intervals vary with sample size, being larger for small sample sizes. Therefore, we
391 included the effect of sample size as a source of heterogeneity among effect sizes, estimated
392 here using within-study sample size.

393

394 **(7) Meta-analyses**

395 We ran multi-level/hierarchical models with the MCMCglmm (Markov chain Monte-
396 Carlo general linear mixed models) function in the MCMCglmm package (Hadfield, 2010), to
397 investigate several types of non-independence. The first is widespread in evolutionary
398 biology, and stems from phylogenetic relatedness among species (Harvey & Pagel, 1991;
399 Nakagawa & Santos, 2012). To control for the potential non-independence of species data

400 points, we implemented phylogenetic information as a variance–covariance matrix in the
401 meta-analyses. As the most recent phylogenetic tree based on 18S rRNA gene sequences
402 comprises only 36 acanthocephalan species (Verweyen *et al.*, 2011), we constructed a new
403 tree based on 59 species (including three new species sequences) (Table S1). We retrieved the
404 distances between species from an ultrametric tree derived from Bayesian inference (see
405 Table S1). In addition to phylogenetic non-independence between effect sizes, we accounted
406 for species- and study-level non-independence by including parasite species and study ID as
407 random factors (Nakagawa & Santos, 2012). Finally, we explored the consequences of
408 violating assumptions of independence among effect size estimates at the individual level
409 (‘shared-measures’ and ‘shared-controls’) by running a sensitivity analysis, following the
410 recommendations of several authors (Koricheva & Gurevitch, 2014; Noble *et al.*, 2017).
411 Shared measures are effect sizes estimated for different traits in the same individuals, shared
412 controls are effect sizes estimated for at least two parasite species using the same control
413 (uninfected) group. We assessed the robustness of the meta-analysis on signed effects of
414 cystacanth infection after controlling for these sources of non-independence, by running the
415 same analysis on a subset of independent measures (Fig. S1B: (i) only one effect size was
416 randomly chosen per individual whenever more than one trait was measured per individual
417 within the same trait category or in two categories besides behaviour, (ii) when one or more
418 behavioural traits were measured together with morphological, physiological or life-history
419 traits on the same individual, we removed the behavioural trait(s) as this category was over-
420 represented in the data set. This was a conservative approach, since behaviour was expected
421 to be the trait category that was most impacted by infection.

422 Effect sizes (Z_r) were used as the dependent variables and their variance was
423 calculated using the formula: $1/(n - 3)$ (Borenstein *et al.*, 2009), where n is the sample size
424 associated with each effect size. The analyses were based on Bayesian hierarchical models

425 which impose definitions of priors (Gelman, 2006). A prior is the strength of belief in the
426 parameter value associated with the variable affecting the observed data. It is represented by
427 the distribution of the parameter based on previous experience. In the absence of information
428 on prior distribution, we used non-informative priors ($nu = 0.002$ and $V = 1$). To assess the
429 influence of these priors on the results, we repeated the analyses with expanded priors ($nu = 1$,
430 $V = 1$, $alpha.mu = 0$, $alpha.V = 1000$), with no detectable effect on our results. For each
431 model, we ran 500,000 iterations which was large enough to minimize the level of
432 autocorrelation (non-independence) between successive iterations: we checked that the
433 autocorrelation coefficient was below 0.10, as suggested by J.D. Hadfield (personal
434 communication). Model convergence was verified according to Gelman & Rubin (1992). To
435 evaluate the reliability of the meta-analytic mean, we also assessed consistency among studies
436 by calculating I^2 , which quantifies heterogeneity between effect sizes for each random factor
437 (Nakagawa & Santos, 2012). I^2 represents the variance accounted for by each random factor
438 relative to the total variance. Heterogeneity was considered as low, moderate and high when I^2
439 = 0.25, 0.50 and 0.75, respectively (Higgins *et al.*, 2003).

440 First, we performed a meta-analysis using signed effect sizes of cystacanth infection,
441 to quantify overall alteration in mean trait value. We also estimated the average magnitude of
442 alterations by estimating the meta-analytic mean of absolute effect sizes on the complete data
443 set, including effect sizes of infection with acanthella. We could not run the meta-analysis
444 directly on absolute values of effect sizes, as the distribution of absolute effect sizes is a
445 folded normal distribution (Morrissey, 2016a). Therefore, we used the procedure
446 recommended by Morrissey (2016a,b), specifically the ‘analyze-then-transform’ approach.
447 We first estimated the meta-analytic mean of all signed effect sizes (all infections with
448 acanthella and cystacanth), and then derived the mean absolute value, we applied the formulae

449 provided by Morrissey *et al.* (2016a) to convert both the posterior mean and confidence
450 interval. The different analysis and their purposes are summarized in Fig. S2.

451

452 **(8) Meta-regressions**

453 We ran a meta-regression to assess the contribution of fixed effects to variation in signed
454 effect sizes of cystacanth infection. The category of trait, infection type (natural or
455 experimental), sample size and year of publication were entered as fixed factors, and parasite
456 species, study and parasite phylogeny as random factors within the model. In the analysis on
457 the entire data set including both acanthella and cystacanth infection to derive the average
458 magnitude of alterations (Fig. S2), parasite developmental stage was added as an additional
459 fixed factor. Since parasite species was already taken into account as a random factor, and
460 was associated with host species (Fig. S1A), neither the host nor the parasite species were
461 considered as fixed factors. We chose to keep these as random factors to control for non-
462 independence between effect sizes. Starting with a global model (including all fixed effects),
463 we performed model selection with the MuMIn package (Bartoń, 2016) using the deviance
464 information criterion (DIC) (Spiegelhalter *et al.*, 2002; Grueber *et al.*, 2011). For each factor
465 level, the meta-analytic mean was estimated from the meta-regression.

466

467 **(9) Analysis of parasite maturity**

468 The aim of this analysis was to test whether the average magnitude and direction of
469 parasite-induced phenotypic alterations varies according to whether parasite developmental
470 stage is, or is not yet, infective to the final host (Fig. S2). First, we assessed to what extent
471 parasite maturity could affect the overall meta-analytic mean of signed effect sizes, by
472 comparing the output of two analyses, the main analysis based the data set restricted to the
473 cystacanth stage, and the additional analysis based on the entire data set (acanthella and

474 cystacanth stages) (Fig. S2). We expected the meta-analytic mean of signed effect sizes to be
475 positive and larger when considering cystacanth infection only compared to both
476 developmental stages. In addition, as for the overall mean absolute value, we derived the
477 mean absolute values of effect sizes and their confidence intervals for each factor level,
478 including parasite developmental stage. We used the ‘analyze-then-transform’ approach on
479 the meta-analytic mean effect size of each factor level estimated from the meta-regression on
480 signed effect sizes (both acanthella and cystacanth included).

481

482 **(10) Publication bias**

483 Statistically significant results are much more likely to be published than non-significant ones
484 (Rosenthal, 1979). In addition, when published, studies reporting non-significant results tend
485 to be based on large sample sizes which is expected to increase their leverage on the meta-
486 analytic mean. We identified potential publication biases using funnel plot (Sterne & Egger,
487 2001). We quantified the magnitude of these publication biases using both Egger’s regression
488 (Egger *et al.*, 1997) and trim-and-fill (Duval & Tweedie, 2000) methods. We estimated the
489 number of missing studies using both L0 and R0 estimators (Duval & Tweedie, 2000). In
490 order to remain conservative, we reported the estimator giving the largest number of missing
491 studies. The associated correction was then applied to the first meta-analytic mean to see if
492 the missing studies would have affected it significantly (Møller & Jennions, 2001; Rothstein,
493 Sutton & Borenstein, 2005).

494 All analyses were run using the R software (version 3.4.3, R Core Team, 2018).

495

496 **III. RESULTS**

497 The full data set comprises 279 effect sizes obtained from 81 studies (Fig. 1), conducted on 13
498 species of acanthocephalan parasites (Table 2A), and 20 host species belonging to three

499 orders of Crustacea and one order of Insecta (Fig. S1A). Our data set was composed of two
500 phylogenetically different acanthocephalan classes: Archiacanthocephala and
501 Palaeacanthocephala. Although these two classes were not equally represented (11% and
502 89%, respectively), we retained both in order to maximize statistical power given the
503 variability in effect size estimates. The fish parasite *Pomphorhynchus laevis* accounted for
504 33% of the total number of effect size estimates, whereas estimates obtained for
505 *Acanthocephalus anguillae*, *Hexaglandula corynosoma* and *Pseudocorynosoma constrictum*
506 accounted for only 2.5% in total (Table 2A, Fig. S1A). Among the different trait categories,
507 behaviour was the most frequently recorded trait, accounting for about 49% of all effect size
508 estimates, whereas morphological traits represented only 9.7% (Table 2B, Fig. S1B). Effect
509 size estimates of vulnerability to predation represented only 5.4% of the data set (Table 2B;
510 Fig. S1B). Most effect sizes were estimated on intermediate hosts infected with the cystacanth
511 stage (261 out of 279) as compared to acanthella (18).

512 Most effect size values were retrieved from studies reporting more than one estimate
513 (93.5% of the overall data set), justifying the incorporation of study as a random factor in the
514 model. Additionally, more than half the data set (58.8% of effect size values) comprised
515 shared measures (55.9% of effect size values), with very few cases of shared controls (2.9%)
516 (Fig. S1B). Shared measures were found in all trait categories except predation.

517

518 **(1) Meta-analytic means and phylogenetic inertia**

519 To incorporate phylogenetic information in the meta-analysis, we first estimated phylogenetic
520 relationships among 59 acanthocephalan species using Bayesian inference of nuclear 18S
521 rDNA sequences. The phylogeny was well resolved (Fig. 2), and our tree topology matches
522 those published previously [see Verweyen *et al.* (2011), and references therein]. We confirmed
523 parphyly of the orders Echinorhynchida and Polymorphida within the most diversified class

524 Palaeacanthocephala, in agreement with Verweyen *et al.* (2011) but with a larger data set (59
525 species instead of 29 species) (Fig. 2).

526 Overall, heterogeneity due to phylogenetic inertia (I^2) accounted for about 12–13% of
527 the variation in signed effect sizes of infection with the cystacanth stage only (Table 3).
528 Incorporating the signed effect sizes of infection with acanthella slightly increased this
529 phylogenetic signal to 19% of overall variation (Table S2A). The meta-analytic mean effect
530 size of infection with the cystacanth stage was significantly positive (0.28 [0.05–0.49], with
531 phylogenetic correction) (Fig. 3). However when incorporating the signed effect sizes of
532 infection with acanthella (entire data set including cystacanth and acanthella infection), the
533 meta-analytic mean was no longer significant (0.23 [–0.19–0.57], with phylogenetic
534 correction) (Fig. S3). Finally, the average magnitude of alteration induced by acanthocephalan
535 infection independently of parasite transmission (absolute mean value) was moderate to large
536 (0.40 [0.34–0.60]) (Fig. 4).

537 We ran another analysis on a subset of 230 signed effect size estimates, after removing
538 ambiguous phenotypic traits with respect to whether an increase or a decrease would enhance
539 parasite transmission in cystacanth-infected hosts. In this analysis, the meta-analytic mean
540 remained significant (0.32 [0.05–0.52]) (Fig. S4).

541 Finally, to account for non-independence among effect size estimates caused by shared
542 measures and shared controls, we ran a sensitivity analysis on a subset of 143 independent
543 effect size estimates: the meta-analytic mean of infection with cystacanths was still significant
544 (0.31 [0.01–0.52]) (Fig. S5).

545

546 **(2) Meta-regressions**

547 To assess whether PIPAs enhance parasite transmission, we focused the meta-regression
548 analysis on signed effect sizes including the cystacanth stage only (Fig. S2). The meta-

549 regression revealed that trait category and sample size were the first factors driving variation
550 in the magnitude of effect sizes, regardless of the incorporation of ambiguous traits (Fig. 3;
551 Table 3), or not (Fig. S4; Table S2B). Specifically, two behavioural traits (response to stimuli
552 and taxis/phobia), one life-history trait (reproduction), one morphological trait (colour), one
553 physiological trait (immunity), and the vulnerability to predation of suitable final hosts, were
554 significantly and positively affected by infection with cystacanths (Fig. 3). Here also,
555 heterogeneity arising from random effects was consistent across models, regardless of the
556 inclusion of fixed effects and their total number in the analyses (Table 3). Among the random
557 effects, study ID accounted for about 32% of heterogeneity in signed effect sizes, whereas
558 parasite species accounted for only 7% (Table 3).

559 The average magnitude of alteration, estimated for each factor as the mean absolute
560 effect size, was comparable between developmental stages. In addition, behavioural and life-
561 history traits seemed to be the most strongly affected ones (Fig. 4).

562

563 **(3) Publication bias**

564 Based on Egger's regression, there was no significant evidence for a publication bias
565 (intercept = 0.05, 95% CI = -0.02-0.11). This was further confirmed by the trim-and-fill
566 analysis. Although 48 effect size estimates were likely to be missing on the left side of the
567 funnel plot (Fig. 5), the funnel plot was almost symmetrical and the correction of -0.09 from
568 the trim-and-fill did not alter the meta-analytic mean significantly (0.26, 95% CI = 0.03-
569 0.45).

570

571 **IV. DISCUSSION**

572 The aim of our study was to undertake a critical review on host manipulation by
573 acanthocephalan parasites, in the framework of phylogenetic meta-analysis. We believe the

574 originality and strength of our analysis lies in several features. First, we ran a phylogenetically
575 corrected meta-analysis using a more exhaustive and multidimensional data set ($N = 279$
576 estimates of effect on a wide range of phenotypic traits) than in previous meta-analyses on the
577 impact of parasites, which focused on the magnitude of behavioural alterations (Nakagawa *et*
578 *al.*, 2015: $N = 202$, including 92 effect sizes from nine acanthocephalan species), on body
579 condition (Sánchez, 2018; $N = 553$), on the relationship between infection and social status in
580 vertebrates (Habig *et al.*, 2018, $N = 128$), or on the relationship between infection and group
581 size (Patterson & Ruckstuhl, 2013; $N = 70$). A key feature of our study is that it incorporated
582 all phenotypic traits reported in order to (i) broaden our understanding of multidimensionality
583 in manipulation by acanthocephalans, and (ii) avoid potential bias resulting from inclusion
584 only of behavioural traits [as in previous studies (Poulin, 1994, 2000; Nakagawa *et al.*,
585 2015)], given that they are more likely to be involved in parasite transmission. Second, we
586 quantified the overall effect of these multiple phenotypic alterations induced by
587 acanthocephalans on parasite transmission by assigning a benefit in terms of increased
588 encounter rate with the final host or decreased energetic expenditure by the intermediate host.
589 We also considered the magnitude of alterations independently from increased parasite
590 transmission. Third, we addressed whether the effect size of infection differs according to trait
591 category and parasite stage, as a way to address how fine-tuned PIPAs are.

592

593 **(1) How strong is the general effect of infection, independent of parasite phylogeny?**

594 We found little evidence for a phylogenetic signal. Relatedness between acanthocephalan
595 species accounted for only a small proportion of the heterogeneity of all effect size estimates.
596 The negligible effect of phylogenetic distance suggests that Acanthocephala is a homogeneous
597 taxon in terms of phenotypic alterations induced in intermediate hosts. This conclusion must

598 however be made with caution, as the class Archiacanthocephala is under-represented in the
599 data set.

600 Overall, acanthocephalan parasites induce low to moderate alterations in their host
601 phenotype, a result in agreement with Poulin (1994). The phylogenetic mean ranges from $r =$
602 0.23 to 0.40, depending on correction for phylogeny and on the use of absolute or signed
603 effect sizes.

604 The meta-regression analysis on signed effect sizes revealed no effect of the type of
605 infection (experimental or natural) on overall intensity of manipulation (Fig. 4). We can
606 therefore confidently rely on results from experimental infections in studies investigating the
607 role of parasite stage (Dianne *et al.*, 2011), parasite age (Franceschi *et al.*, 2008), parasite and
608 host populations (Franceschi *et al.*, 2010b), abiotic factors (Labaude, 2017a), and biotic
609 factors (no to date, but see Fayard *et al.*, 2019) in modulating the intensity of PIPAs. In
610 addition, the intensity of PIPAs decreased with increasing sample size. This highlights the
611 importance of the number of replicates within a study in estimating the magnitude of PIPA.

612 Among random factors, the meta-regression analysis on signed effect size revealed a
613 negligible effect of parasite species on overall intensity of manipulation, but a more important
614 effect of study. This study effect highlights the possible impact of differences in experimental
615 designs in estimating the type and magnitude of PIPAs.

616

617 **(2) Is there evidence for adaptive manipulation? Trophic transmission and parasite stage**

618 For the mature parasite stage (cystacanth only), acanthocephalans do induce a moderate
619 increase in traits affecting parasite transmission to the definitive host. However, there are still
620 too few studies quantifying trophic transmission (only 5.4% of the cystacanth data set), in
621 comparison to those reporting PIPAs. In addition, even fewer studies have actually attempted
622 to estimate the contribution of a given altered trait to trophic transmission (Kaldonski *et al.*,

623 2009; Perrot-Minnot *et al.*, 2012; Jacquin *et al.*, 2014). This limitation should not be
624 overlooked when reviewing evidence for adaptive manipulation.

625 Another line of evidence for adaptive manipulation is a trend for reversed parasite-
626 induced alterations in the intermediate host between parasite developmental stages, predicted
627 theoretically to enhance parasite infectivity to the final host (Parker *et al.*, 2009). The average
628 magnitude of alterations induced by infection with acanthella was comparable to that induced
629 by infection with cystacanth, but in the opposite direction (Fig.4; Fig. S3). This suggests that
630 the acanthella stage could have a real and opposite impact on host phenotype compared to the
631 cystacanth stage, in ways that are likely to decrease the vulnerability to predation of the
632 infected intermediate host (Parker *et al.*, 2009; Dianne *et al.*, 2011). This result must be
633 considered with caution, however, given the low number of effect size estimates for the
634 acanthella stage ($n = 18$) compared to the cystacanth stage ($n = 261$), and the low number of
635 parasite species for which estimates were available (five). In addition, half of these effect
636 sizes were estimated for behavioural traits (taxis/phobia, protection, and response to stimuli),
637 which might lead to overestimated differences between acanthella infection and cystacanth
638 infection. Indeed, while acanthella and cystacanths are theoretically likely to have opposing
639 effects in terms of behavioural alterations (Parker *et al.*, 2009), energy-saving strategies, such
640 as physiological or behavioural castration or immunosuppression, are expected to be shared
641 by both parasite stages to some extent. However, while immunosuppression may allow energy
642 conservation, it may also compromise the survival of infected hosts in response to other
643 pathogens (Cornet *et al.*, 2009). Therefore, immunosuppression might represent a more costly
644 strategy for the acanthella than for the cystacanth stage, given the longer developmental time
645 required to reach the stage infective for the final host (Crompton & Nickol, 1985).
646 Unfortunately, there have been no studies that quantify acanthella-infected host

647 immunocompetence. Finally, there is only mixed evidence in support of an energy-saving
648 strategy by depressing host reproduction at the acanthella stage (Bailly *et al.*, 2018).

649

650 **(3) Is there evidence for multidimensional alterations?**

651 Overall, all trait categories were impacted by cystacanth infection. Behaviour was the
652 trait category that was most significantly impacted, and hence is the category expected to
653 contribute the most to acanthocephalan transmission (Fig. 3). Taxis/phobia was the most
654 strongly impacted subcategory, followed by response to stimuli. If reversed taxis can drive
655 alterations in microhabitat preferences through alterations in reactions to light, gravity, air or
656 water velocity, or substrate, the observed pattern is likely to increase the encounter rate of the
657 cystacanth with final hosts. These findings confirm that altering the host's microhabitat
658 preference is an important feature of manipulation by acanthocephalans compared with other
659 trophically transmitted parasites, whereas activity is not significantly affected (Lafferty &
660 Shaw, 2013). Changes in responses to stimuli are also expected to modulate the encounter rate
661 of infected prey and the final hosts. More surprising is the non-significant effect of cystacanth
662 infection on protection behaviour (i.e. on exposure). However, we included studies that scored
663 protection/exposure behaviour under simulated predation threat in the 'response to stimuli'
664 subcategory, meaning that those in the 'protection/exposure' subcategory of behaviour
665 reported alterations in protective behaviour solely in the absence of predation risk. The
666 mechanisms by which acanthocephalans alter these context-dependent traits may thus rely on
667 stimulus perception/response, rather than on avoidance or defensive behaviour itself.

668 Among physiological and life-history-related traits, only host immunity and
669 reproduction were significantly impacted by infection with cystacanth stages (Fig. 3). We
670 interpret immunosuppression and castration as part of an energy-saving strategy to support
671 both host maintenance and parasite growth, thereby increasing host survival and indirectly,

672 parasite transmission. Alternatively and non-exclusively, alterations in host reproductive and
673 immune system traits could be linked to behavioural alterations, and thereby to parasite
674 transmission. The immune and nervous systems are connected through several different
675 pathways in animals (Dantzer *et al.*, 2008; Adamo, 2013). Neurological functions can be
676 modulated by immune factors such as cytokines by means of specific neuronal receptors.
677 Cytokines released by the immune system act as signalling molecules to the central nervous
678 system, and can result in sickness behaviour: a set of physiological and behavioural
679 alterations that promote the survival of infected individuals (Dantzer, 2004; Dantzer & Kelley,
680 2007). Adamo (2013) postulated that if parasites could alter the amount or the type of
681 cytokines released by the host immune system, then this could result in abnormal behaviour.
682 Although highly interesting, this neuropsychimmune hypothesis has not yet been addressed.

683

684 **(4) Recommendations for future research**

685 Our findings highlights several ways to improve our understanding of the adaptive
686 significance of host manipulation. First, for future meta-analysis, researchers should attempt
687 to increase the power and functionality of the metrics used to quantify phenotypic alterations.
688 This could be achieved by increasing sample size, and by reporting effect sizes rather than
689 statistical metrics. Indeed, 85 studies had to be excluded (Fig. 1) from the present analysis
690 because suitable data were not provided or were no longer available. Second, as a
691 consequence of the historical focus on behavioural trait alterations expected to increase
692 trophic transmission of the infective stage, traits not directly related to predator-prey
693 interactions have received little attention in acanthocephalans (Cézilly & Perrot-Minnot,
694 2010), including phenotypic alterations induced by acanthella. Yet, these remain crucial to
695 developing a better understanding of whether PIPAs constitute a ‘manipulation syndrome’,
696 and whether the adaptive value of PIPAs extends to developmental stages not infective to the

697 final host (protective manipulation). Third, studies quantifying actual trophic transmission are
698 still rare (Poulin & Maure, 2015). This is likely due to the fact that designing studies to
699 quantify trophic transmission raises practical challenges, in particular under field conditions,
700 as either prey choice or the diet of final hosts needs to be analysed [see Cézilly *et al.* (2010),
701 for a recent review]. The study of proximate mechanisms, in particular the
702 neuropsychimmune hypothesis of parasite manipulation, also requires attention (Poulin &
703 Maure, 2015). Finally, taxonomic bias may arise from focusing on only a small set of model
704 species (Poulin & Maure, 2015). In our data set, the most diverse and derived class
705 Palaeacanthocephala was over-represented, while the more ancient class Archiacanthocephala
706 was represented by only two species (*Moniliformis moniliformis* and *Oncicola venezuelensis*).
707 This prevented a detailed comparison between these two classes, for example to investigate
708 whether host manipulation increases over evolutionary time.

709 Finally, another stimulating area in the study of parasite manipulation from an
710 evolutionary point of view is to investigate not only the magnitude of parasite manipulation
711 (changes in trait means) but also alterations in trait variability. Behavioural variability is
712 predicted to decrease in infected hosts, making them more susceptible to predators as part of
713 the manipulation strategy (Nakagawa *et al.*, 2015). Alternatively, behavioural variability in
714 infected hosts could increase as a consequence of parasite-induced disruption of regulatory
715 pathways controlling behaviour. To our knowledge, only one meta-analytic study has
716 quantified the effect size of infection on behavioural variability and they failed to find a
717 significant effect (Nakagawa *et al.*, 2015). However, their study was not restricted to
718 acanthocephalans, and it remains possible that other taxa of parasites could respond
719 differently, both in mean host traits and also their variance.

720

721 **V. CONCLUSIONS**

722 (1) Overall, infection with acanthocephalans induces low to moderate phenotypic alterations
723 in their hosts. The magnitude of alterations induced by the infective stage was highest for
724 behavioural traits related to microhabitat choice and response to stimuli, and for immunity
725 and reproduction. Although a trend for opposite effects of infection with acanthella was
726 detected, a thorough analysis of the "predation suppression then predation enhancement"
727 strategy is still limited by the lack of data at the acanthella stage of development.
728 Furthermore, testing for publication bias showed that 48 data points were lacking,
729 corresponding to negative effects (opposing parasite-induced transmission facilitation),
730 although no significant publication bias was detected overall. Future studies should be careful
731 not to censor negative evidence for the host manipulation hypothesis.

732 (2) Multidimensionality of parasite manipulation was indicated in the significant effect of
733 infection on all trait categories. Questions remain regarding the links between behavioural,
734 life-history, and physiological traits. For instance, testing of the neuropsychimmune
735 hypothesis has so far been restricted to establishing correlations between phenotypic
736 responses (phototaxis and immunity) in few acanthocephalan species (Cornet *et al.*, 2009).
737 Although informative from an ecological point of view, this is not a powerful mechanistic
738 approach since the absence of a phenotypic correlation does not prove the existence of
739 independent modulation of these traits. Manipulating the level of immunocompetence, and
740 monitoring any resulting alterations in levels of brain neuromodulators, neurogenesis or
741 neuronal apoptosis, would be a more promising way to decipher the interrelationships
742 between the immune and neural systems, and any consequences on behaviour.

743 (3) Although we were able to detect low to moderate increases in traits promoting parasite
744 transmission to the definitive host, there are still too few studies that actually quantify trophic
745 transmission. Even fewer have attempted to understand the relationship between

746 multidimensional phenotypic alterations and parasite transmission success (discussed in
747 Cézilly & Perrot-Minnot, 2010; Thomas *et al.*, 2010).

748 (4) To allow comparison of effect sizes between trait categories, we combined traits that were
749 functionally comparable from an ecological viewpoint. The criteria used here to assign
750 phenotypic traits to different categories may be more broadly applicable to a wide range of
751 host species. As a theoretical approach to host manipulation by parasites is relevant across a
752 diverse range of taxonomic groups (Thomas *et al.*, 2012; Lafferty & Shaw, 2013), our method
753 may be applicable to many other parasites engaged in host manipulation.

754 (5) The past 10 years has seen a decreasing number of empirical studies relative to theoretical
755 analyses and reviews, creating an “imbalance between facts and ideas” (Poulin & Maure,
756 2015). This review provides quantitative evidence that the fascinating phenomenon of host
757 manipulation has solid theoretical and empirical foundations, but also raises challenging
758 questions about the underlying proximate and ultimate mechanisms that call for broader
759 methodological and taxonomic coverage.

760

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770

771 **Authorship:** M.F. and M.-J. P.-M. designed project goals, trait categorization, and collected
772 the data. M. F. and F.-X. D.-M. run the meta-analysis, R.W. and M.-J. P.-M. collected and
773 analysed molecular data for phylogenetic reconstruction, and drafted the relevant section. M.
774 F., F.-X. D.-M and M.-J. P.-M. drafted the manuscript. All authors revised the manuscript.

775

776 **Data Accessibility Statement:** Data and R script for the meta-analysis are available on
777 Mendeley repository at DOI: 10.17632/k5y4g5nfwy.1

778

779

780 **VII. REFERENCES**

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1326 **VIII. SUPPORTING INFORMATION**

1327 Additional supporting information may be found in the online version of this article.

1328 **Table S1.** List of acanthocephalan species included in the phylogenetic analysis, and the
1329 outgroup species (*Seison nebaliae*, Rotifera), with their accession numbers.

1330 **Fig. S1.** Number of effect size estimates retrieved from published studies on the impact of
1331 acanthocephalan infection on their intermediate invertebrate hosts.

1332 **Appendix S1.** Phylogenetic relationship of acanthocephalans based on 18S ribosomal gene
1333 sequences.

1334 **Fig. S2.** Road map of the analyses.

1335 **Table S2.** Composition of the meta-analytic models in the complementary analysis.

1336 **Fig. S3.** Parasite-induced alterations of mean trait value, incorporating all parasite
1337 developmental stages: forest plot from the complementary analysis with global meta-analytic
1338 mean of signed effect sizes (overall), and the meta-analytic mean for each moderator
1339 (categories and subcategories of traits, parasite maturity and type of infection).

1340 **Fig. S4.** Ambiguous traits: forest plot with global meta-analytic mean of signed effect sizes
1341 (overall), and the meta-analytic mean for each moderator (categories and subcategories of
1342 traits and type of infection).

1343 **Fig. S5.** Sensitivity analysis to account for the non-independence of effect sizes: forest plot
1344 with global meta-analytic mean of signed effect sizes (overall), and the meta-analytic mean
1345 for each moderator (categories of traits and type of infection).

1346 Table 1. Categories of host trait altered by acanthocephalan parasites that were incorporated in the meta-analysis. The predicted direction of
 1347 alteration under the hypothesis of increased trophic transmission of the infective cystacanth stage to definitive hosts is provided as the main
 1348 hypotheses. The direction of alteration is predicted from either increased encounter rate between infected prey and predators (ERH: encounter
 1349 rate hypothesis), or decreased energetic expenditure by intermediate host (ESH: energy-saving hypothesis). In the former case, parasite-induced
 1350 phenotypic alteration (PIPA) results in predation bias towards infected hosts. Non-exclusively in the latter case, energy saving/reallocation
 1351 increases host and parasite survival and/or parasite growth rate.

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Host trait category	Host trait subcategory	Main hypothesis	Competing hypothesis (opposite signed effect)
Behaviour	Activity	Higher activity increases conspicuousness; distance covered increases the probability of encounter (ERH)	Lower activity increases catchability (ERH) and saves energy (ESH)
	Protection	Decreased protective behaviour, increased exposure (ERH)	
	Response to stimuli	Decreased detection of stimulus or responsiveness to predator cues (ERH)	
	Taxis/phobia	Micro-habitat overlap with predators (decreased photophobia or negative geotaxis) (ERH)	
Life history	Body condition	Increased body condition (ERH and ESH)	

	Foraging	Higher exploration for resources (high food intake) increases prey exposure to predators (ERH)	
	Reproduction	Behavioural (male) and physiological (female) castration (ESH)	
	Intraspecific interaction (sociality)	Decreased agonistic behaviours (competition, cannibalism) (ESH)	
	Survival	Higher host survival increases the time frame for transmission (ERH and ESH)	
Morphology	Colour	Increased conspicuousness (ERH)	
	Growth	Higher growth/body size increases detection (ERH)	
Physiology	Immunity/resistance	Immunosuppression (ESH)	
	Energy reserves/metabolism	Higher energetic reserves (ERH and ESH) Lower metabolic rate (decreased oxidative stress: increased survival) (ERH and ESH)	Higher metabolic rate (sustains higher foraging and activity rate) (ERH and ESH)
	Neurophysiology	High serotonin level decreases anxiety (ERH) – associated with low dopamine level (5HT-DA opponency)	Low serotonin level impairs aversive learning, hence delays response to predation stimulus (ERH) – associated with high dopamine level (5HT-DA opponency)

Predation	Non-host	Decreased predation by non-hosts (ERH)
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	Suitable final host	Increased predation by suitable hosts (ERH)
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Table 2. Number of studies and number of effect size estimates including both cystacanth and acanthella infection stages (with number of effect sizes for acanthella infections alone shown in parentheses) included in our data set for (A) acanthocephalan parasite species and (B) categories and subcategories of host phenotypic traits.

A			
Parasite class	Parasite species	Number of studies	Number of effect sizes (acanthella only)
Archiacanthocephala	<i>Moniliformis moniliformis</i>	8	26 (0)
	<i>Oncicola venezuelensis</i>	2	5 (0)
Palaeacanthocephala	<i>Acanthocephalus anguillae</i>	1	2 (0)
	<i>Acanthocephalus dirus</i>	18	29 (2)
	<i>Acanthocephalus lucii</i>	12	25 (1)
	<i>Echinorhynchus truttae</i>	6	9 (0)
	<i>Hexaglandula corynosoma</i>	1	2 (0)
	<i>Leptorhynchoides thecatus</i>	1	8 (0)
	<i>Plagiorhynchus cylindraceus</i>	3	7 (0)
	<i>Polymorphus minutus</i>	27	56 (4)
	<i>Pomphorhynchus laevis</i>	39	92 (10)
	<i>Pomphorhynchus tereticollis</i>	7	15 (0)
	<i>Pseudocorynosoma constrictum</i>	2	3 (1)
TOTAL			279 (18)
B			
Trait category	Trait subcategory	Number of studies	Number of effect sizes (acanthella only)
Behaviour	Activity	17	19 (1)
	Protection	15	23 (2)
	Response to stimuli	22	43 (4)
	Taxis/phobia	26	53 (2)
Life history	Body condition	4	4 (0)
	Foraging	4	8 (1)
	Reproduction	10	25 (3)
	Intraspecific interaction	1	1 (0)
	Survival	5	6 (1)
Morphology	Colour	5	7 (0)
	Growth	14	20 (3)
Physiology	Immunity/resistance	8	27 (0)
	Energy reserves/metabolism	12	19 (0)

	Neurophysiology	5	9 (0)
Predation	Suitable final host	10	13 (0)
	Non-host	2	2 (0)
TOTAL			279 (18)

Table 3. Composition of the meta-analytic models run to explain variation in signed effect sizes of infection with cystacanths only. The corresponding deviance information criterion (DIC), and heterogeneity (I^2) arising from the random factors (study, parasite species and parasite phylogenetic distance) are provided. The best model, according to the lowest DIC, is shown in bold type.

Model	Moderators (fixed effects)	DIC	Heterogeneity I^2 (%) (random effects)		
			Parasite species	Study	Parasite phylogenetic distance
1	intercept only	215.36	6.55	31.18	11.84
2	category of traits	208.20	6.45	32.78	13.60
3	infection type	215.77	6.61	30.56	13.12
4	publication year	216	7.05	30.38	12.39
5	sample size	209.80	6.40	32.70	11.86
6	category of traits + sample size	202.99	6.42	34.74	13.20
7	category of traits + infection type + publication year + sample size	204.68	6.71	34.62	14.04

FIGURE LEGENDS

Fig. 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram (Liberati *et al.*, 2009; Nakagawa *et al.*, 2017) for this meta-analysis on variation in the intensity of host manipulation by acanthocephalans.

Fig. 2. Phylogenetic reconstruction of the phylum Acanthocephala based on 18S rRNA sequences from 59 species, and one outgroup species of Rotifera (in black), using Bayesian MCMC algorithms with MrBayes. Species included in the meta-analyses belong to the classes Archiacanthocephala (in brown, two species) and Palaeacanthocephala (in blue, 11 species). Species identified with one, two or three asterisks are represented in the data set by less than 5, between 5 and 15, or more than 15 estimates, respectively. Black and grey dots represent values of posterior probabilities higher than 0.90 and 0.80, respectively.

Fig. 3. Forest plots of the global meta-analytic mean of signed effect sizes (overall) based on cystacanth-induced alterations in host phenotype, and the meta-analytic mean for each moderator (categories and subcategories of traits and type of infection). Positive effect sizes represent infection-induced alterations of trait value expected to increase trophic transmission, whereas negative effect sizes represent infection-induced alterations expected to decrease trophic transmission. *n*, sample size.

Fig. 4. Forest plots of the global meta-analytic mean of absolute effect sizes (overall), and the meta-analytic mean for each moderator (categories of traits, parasite maturity and type of infection) representing the magnitude of alterations induced by infection with acanthocephalans (both acanthella and cystacanth) on host phenotype. *n*, sample size.

Fig. 5. Funnel plots of (A) original data points (effect size estimates) and (B) residuals from model 1 (Table 3), plotted against precision (the inverse of standard error). Bold lines represent the meta-analytic mean in A and the correction (calculated using the trim-and-fill method) in (B).

Fig.1

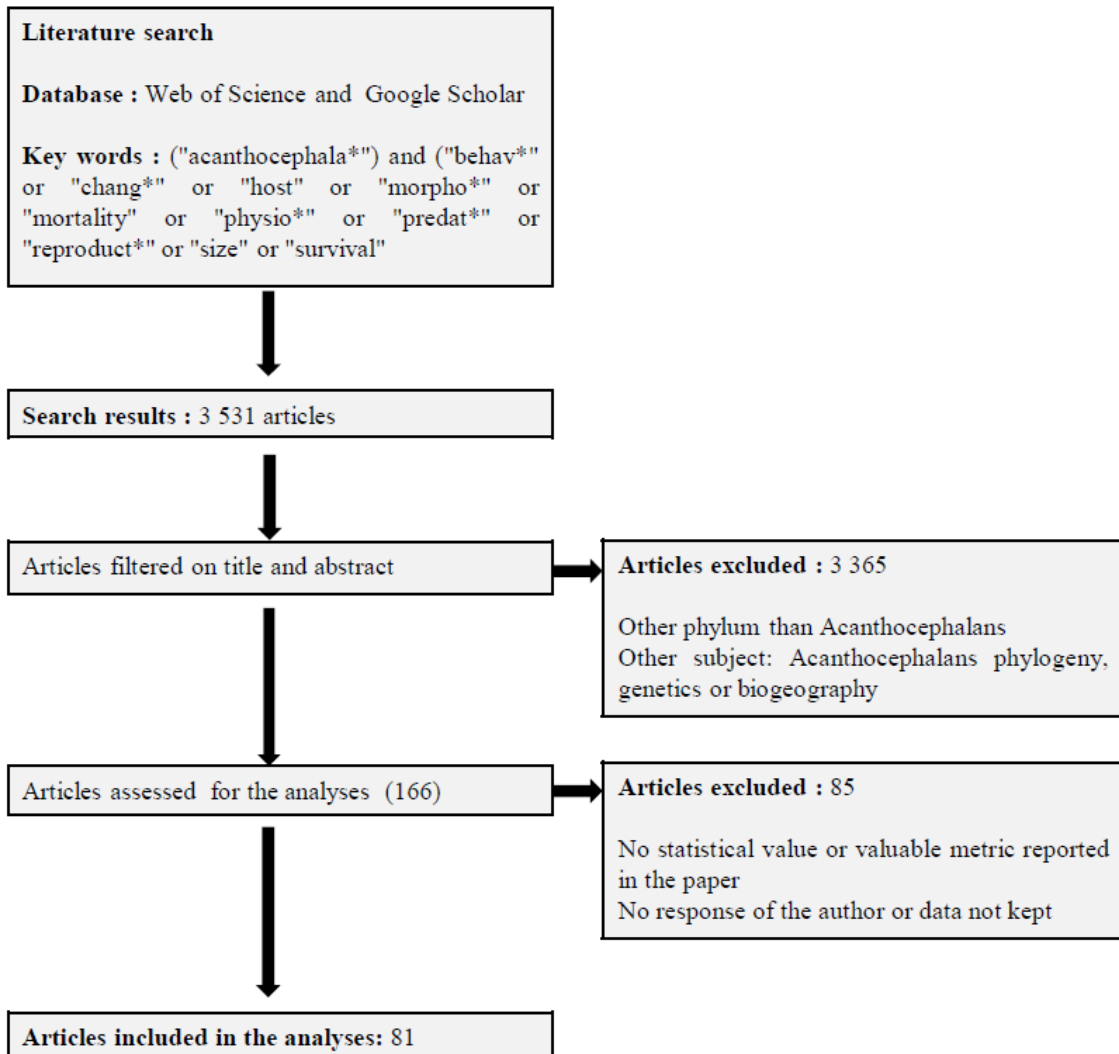


Fig. 2

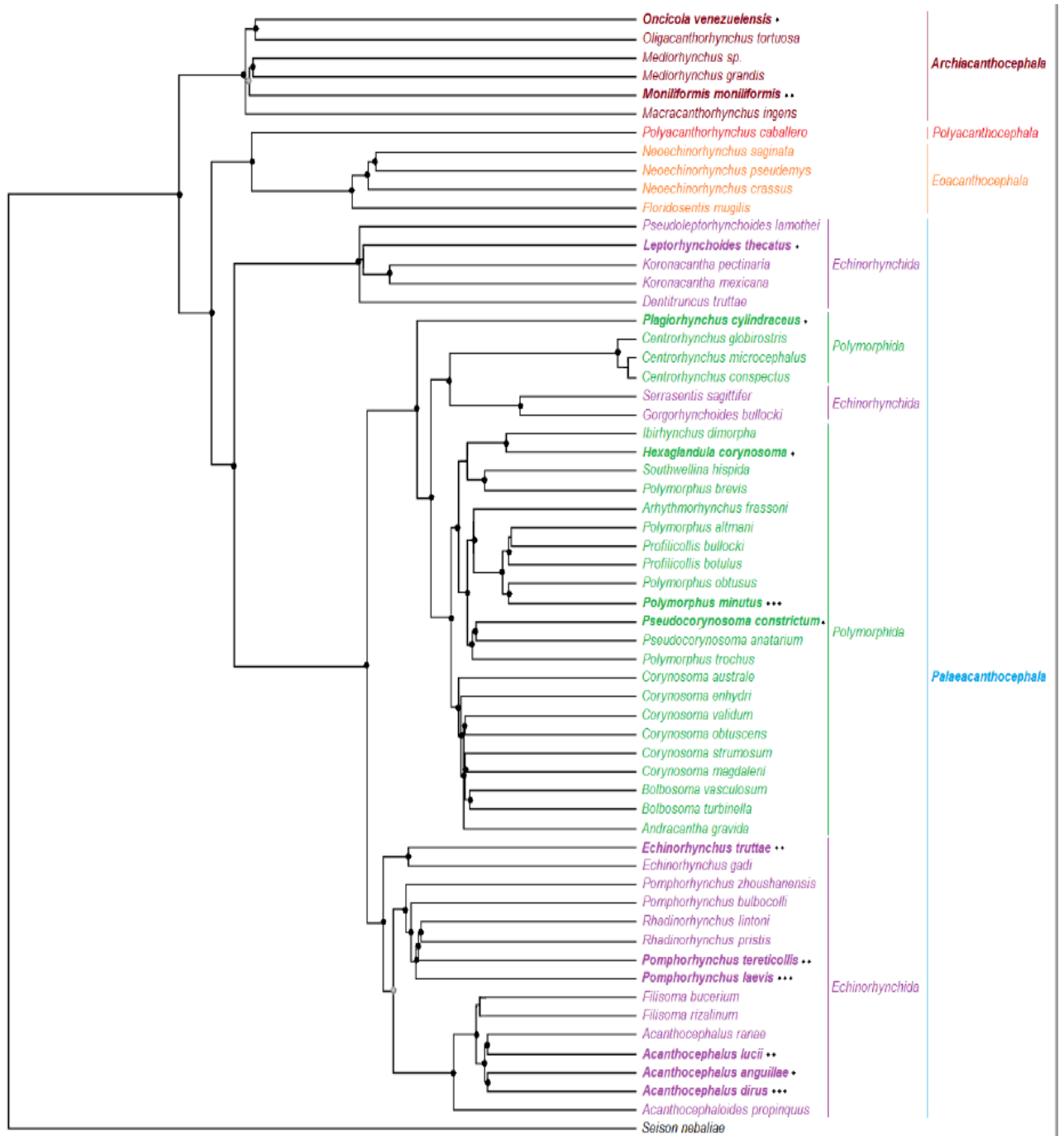


Fig. 3

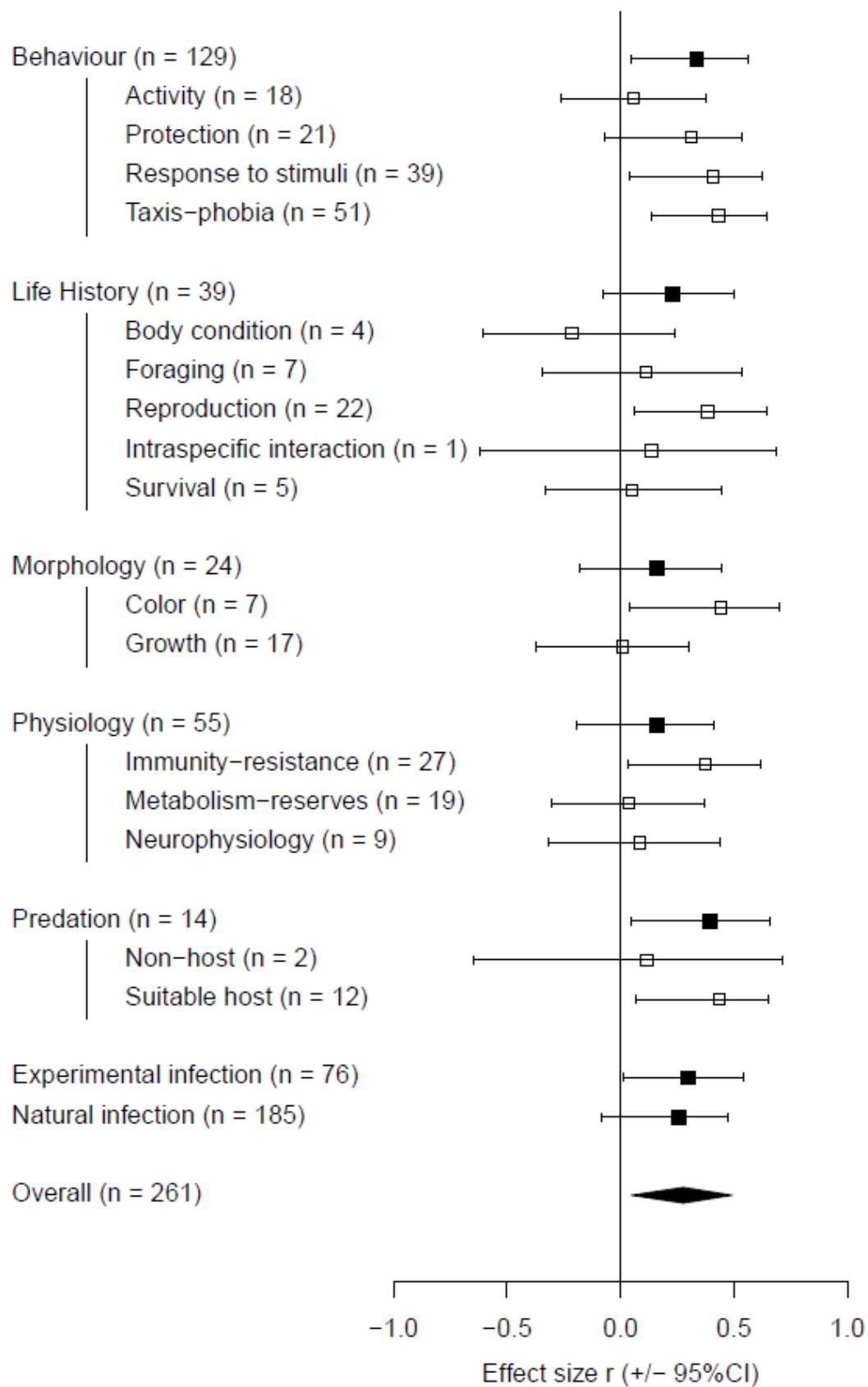


Fig. 4

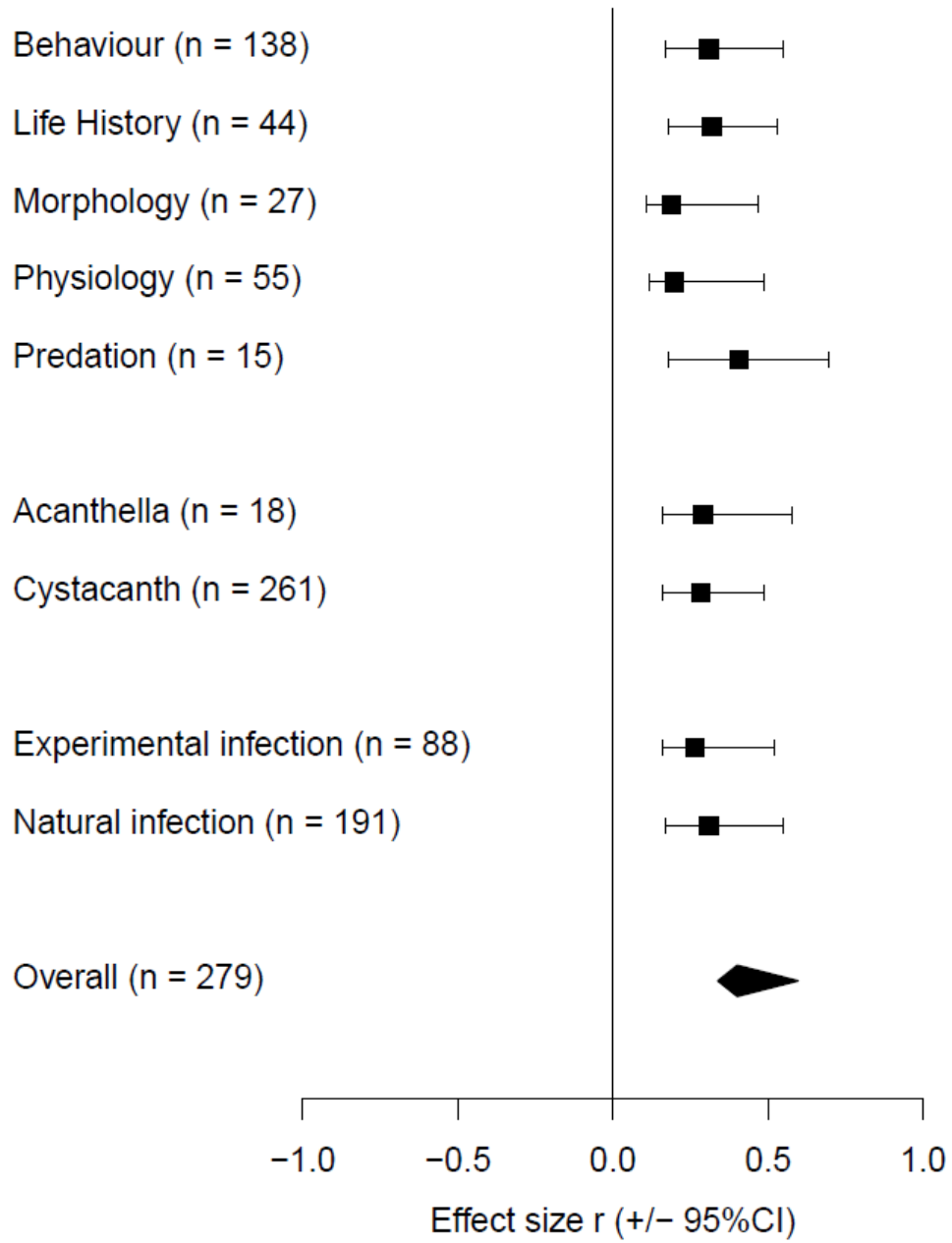
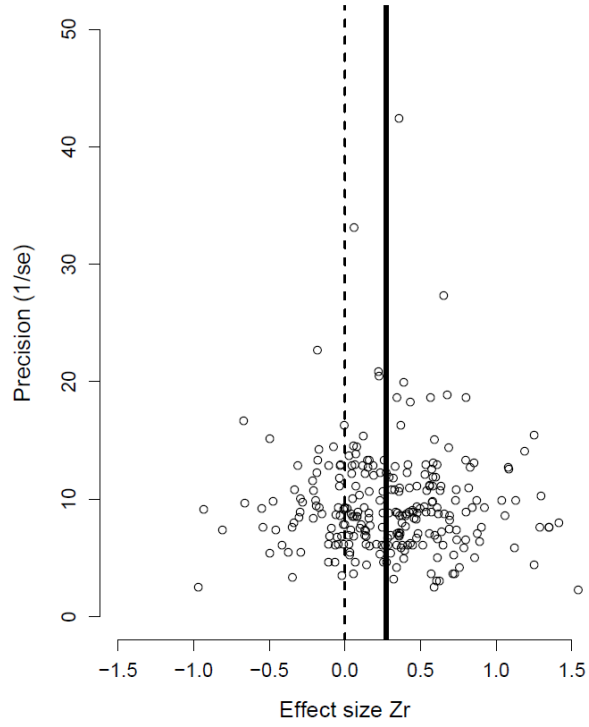


Fig.5

a)



(b)

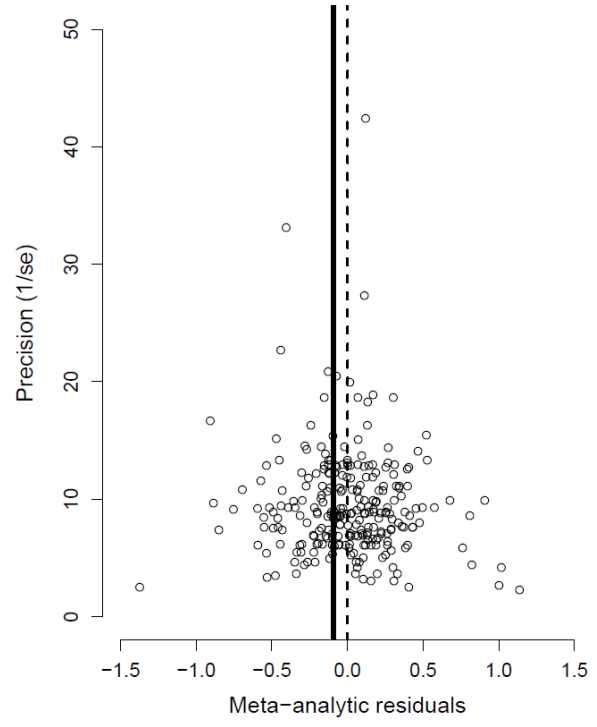
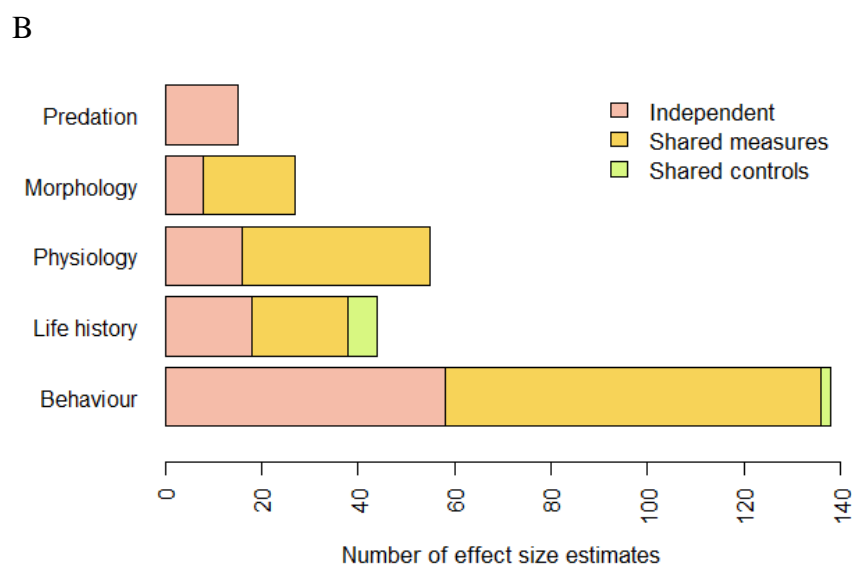
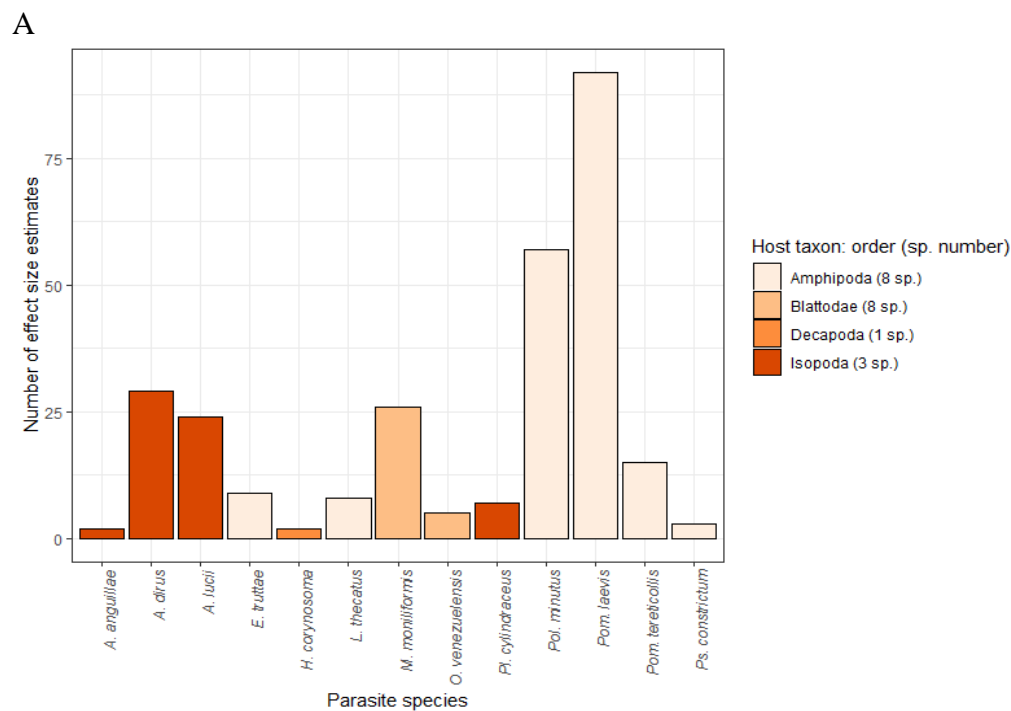


Table S1. List of acanthocephalan species included in the phylogenetic analysis ($N = 59$) and the outgroup species (*Seison nebaliae*, Order Seisonacea, Phylum Rotifera), with their accession numbers. The 18S sequences of *Acanthocephalus anguillae*, *Acanthocephalus ranae* and *Pomphorhynchus bulbocolli* were produced as part of the present study, all others were retrieved from Genbank. Accession number for the outgroup species *Seison nebaliae* is DQ089737.

Genbank accession no.	Species	Order	Class within Acanthocephala phylum
AF001844	<i>Macracanthorhynchus ingens</i>	Oligacanthorhynchida	Archiacanthocephala
AF001843	<i>Mediorhynchus grandis</i>	Gigantorhynchida	Archiacanthocephala
AF064816	<i>Mediorhynchus</i> sp.	Gigantorhynchida	Archiacanthocephala
HQ536017	<i>Moniliformis moniliformis</i>	Moniliformida	Archiacanthocephala
AF064817	<i>Oligacanthorhynchus tortuosa</i>	Oligacanthorhynchida	Archiacanthocephala
AF064818	<i>Oncicola</i> sp.	Oligacanthorhynchida	Archiacanthocephala
AF388660	<i>Polyacanthorhynchus caballeroi</i>	Polyacanthorhynchida	Polyacanthocephala
AF064811	<i>Floridosentis mugilis</i>	Neoechinorhynchida	Eoacanthocephala
AF001842	<i>Neoechinorhynchus crassus</i>	Neoechinorhynchida	Eoacanthocephala
U41400	<i>Neoechinorhynchus pseudemydis</i>	Neoechinorhynchida	Eoacanthocephala
AY830150	<i>Neoechinorhynchus saginata</i>	Neoechinorhynchida	Eoacanthocephala
AY830149	<i>Acanthocephaloides propinquus</i>	Echinorhynchida	Palaeacanthocephala
LS991432	<i>Acanthocephalus anguillae</i>	Echinorhynchida	Palaeacanthocephala
AY830151	<i>Acanthocephalus dirus</i>	Echinorhynchida	Palaeacanthocephala
AY830152	<i>Acanthocephalus lucii</i>	Echinorhynchida	Palaeacanthocephala
LS991433	<i>Acanthocephalus ranae</i>	Echinorhynchida	Palaeacanthocephala
JX460866	<i>Dentitruncus truttae</i>	Echinorhynchida	Palaeacanthocephala
JX014222	<i>Echinorhynchus gadi</i>	Echinorhynchida	Palaeacanthocephala
AY830156	<i>Echinorhynchus truttae</i>	Echinorhynchida	Palaeacanthocephala
AF064814	<i>Filisoma bucerium</i>	Echinorhynchida	Palaeacanthocephala
JX014229	<i>Filisoma rizalinum</i>	Echinorhynchida	Palaeacanthocephala
AY830154	<i>Gorgorhynchoides bullocki</i>	Echinorhynchida	Palaeacanthocephala
AY830157	<i>Koronacantha mexicana</i>	Echinorhynchida	Palaeacanthocephala
AF092433	<i>Koronacantha pectinaria</i>	Echinorhynchida	Palaeacanthocephala
AF001840	<i>Leptorhynchoides thecatus</i>	Echinorhynchida	Palaeacanthocephala
AY423346	<i>Pomphorhynchus laevis</i>	Echinorhynchida	Palaeacanthocephala
AY423347	<i>Pomphorhynchus tereticollis</i>	Echinorhynchida	Palaeacanthocephala
KY490051	<i>Pomphorhynchus zhoushanensis</i>	Echinorhynchida	Palaeacanthocephala
LS991434	<i>Pomphorhynchus bulbocolli</i>	Echinorhynchida	Palaeacanthocephala
EU090950	<i>Pseudoleptorhynchoides lamothei</i>	Echinorhynchida	Palaeacanthocephala

JX014224	<i>Rhadinorhynchus lintoni</i>	Echinorhynchida	Palaeacanthocephala
JX014226	<i>Rhadinorhynchus pristis</i>	Echinorhynchida	Palaeacanthocephala
JX014227	<i>Serrasentis sagittifer</i>	Echinorhynchida	Palaeacanthocephala
EU267802	<i>Andracantha gravida</i>	Polymorphida	Palaeacanthocephala
JX442165	<i>Arhythmorhynchus frassoni</i>	Polymorphida	Palaeacanthocephala
JX442166	<i>Bolbosoma turbinella</i>	Polymorphida	Palaeacanthocephala
JX014225	<i>Bolbosoma vasculosum</i>	Polymorphida	Palaeacanthocephala
U41399	<i>Centrorhynchus conspectus</i>	Polymorphida	Palaeacanthocephala
KM588206	<i>Centrorhynchus globirostris</i>	Polymorphida	Palaeacanthocephala
AF064813	<i>Centrorhynchus microcephalus</i>	Polymorphida	Palaeacanthocephala
JX442168	<i>Corynosoma australe</i>	Polymorphida	Palaeacanthocephala
AF001837	<i>Corynosoma enhydri</i>	Polymorphida	Palaeacanthocephala
EU267803	<i>Corynosoma magdaleni</i>	Polymorphida	Palaeacanthocephala
JX442169	<i>Corynosoma obtuscens</i>	Polymorphida	Palaeacanthocephala
EU267804	<i>Corynosoma strumosum</i>	Polymorphida	Palaeacanthocephala
JX442170	<i>Corynosoma validum</i>	Polymorphida	Palaeacanthocephala
EU267808	<i>Hexaglandula corynosoma</i>	Polymorphida	Palaeacanthocephala
GQ981436	<i>Ibirhynchus dimorpha</i>	Polymorphida	Palaeacanthocephala
AF001839	<i>Plagiorhynchus cylindraceus</i>	Polymorphida	Palaeacanthocephala
AF001838	<i>Polymorphus altmani</i>	Polymorphida	Palaeacanthocephala
JX442171	<i>Polymorphus brevis</i>	Polymorphida	Palaeacanthocephala
EU267806	<i>Polymorphus minutus</i>	Polymorphida	Palaeacanthocephala
JX442172	<i>Polymorphus obtusus</i>	Polymorphida	Palaeacanthocephala
JX442173	<i>Polymorphus trochus</i>	Polymorphida	Palaeacanthocephala
EU267805	<i>Proflicollis botulus</i>	Polymorphida	Palaeacanthocephala
JX442174	<i>Proflicollis bullocki</i>	Polymorphida	Palaeacanthocephala
EU267801	<i>Pseudocorynosoma anatarium</i>	Polymorphida	Palaeacanthocephala
EU267800	<i>Pseudocorynosoma constrictum</i>	Polymorphida	Palaeacanthocephala
EU267807	<i>Southwellina hispida</i>	Polymorphida	Palaeacanthocephala

Fig. S1. Number of effect size estimates retrieved from published studies on the impact of acanthocephalan infection on their intermediate invertebrate hosts: (A) per host taxon (order) within each acanthocephalan species; (B) according to the source of non-independence between measures and for each host trait category. ‘Shared measures’ are effect sizes estimated on the same individuals but for different traits; ‘shared controls’ are effect sizes estimated for at least two parasite species using the same control group.



Appendix S1. Phylogenetic relationship of acanthocephalans based on 18S ribosomal gene sequences

We retrieved the distances between species from an ultrametric tree derived from a Bayesian inference based on 59 acanthocephalan 18S rRNA gene sequences and using a rotifer as an outgroup (Table S1).

18S rDNA gene sequences

Sequences from 56 acanthocephalan species were retrieved from GenBank. Sequences from three other species for which effect sizes were included in the data set were added (Table S1). Samples of *Acanthocephalus anguillae* and *Acanthocephalus ranae* were collected from the freshwater isopod *Asellus aquaticus*, in the river Ouche (La Colombière, Dijon) in 2004; samples of *Pomphorhynchus bulbocolli* were provided by Dr Spakulova. DNA extraction, amplification of a portion of 18S rDNA, purification of Polymerase Chain Reaction (PCR) products and sequencing, were done following Perrot-Minnot (2004). Three pairs of primers were used to obtain three overlapping sequences. These were assembled into a single sequence of approximately 1700 base pairs (bp) using BioEdit editor (Hall, 1999).

Phylogenetic analysis

Sequences were aligned using MAFFT7.388 software (Katoh & Stanley, 2013), with the E-IONS-I algorithm using the legacy gap penalty option. The best-fitting model of nucleotide substitution was determined using JModelTest-2.1.10. (Darriba *et al.*, 2012) as being the General Time Reversible (GTR) with gamma-distributed rate heterogeneity (G) and a significant proportion of invariable sites (I) model. Bayesian phylogeny reconstruction was

performed with MrBayes (Huelsenbeck & Ronquist, 2001). Four heated chains were run, each one million iterations long, sampled every 200 iterations. The runs reached satisfactory effective sampling sizes ($ESS > 200$). The 50% majority-rule consensus tree was constructed after the removal of a 10% burn-in phase.

Fig. S2. Road map of the analyses. Diagram presenting the five analyses, using either signed effect sizes (the alteration of mean trait value, including the direction of change favouring parasite transmission) or absolute effect sizes (the magnitude of phenotypic alteration), and incorporating both parasite stages or only cystacanth infection. Two final analyses were run after excluding trait alterations for which the consequence on trophic transmission (sign) could not be unambiguously assigned, and trait alterations for which estimates were not independent (sensitivity analysis).

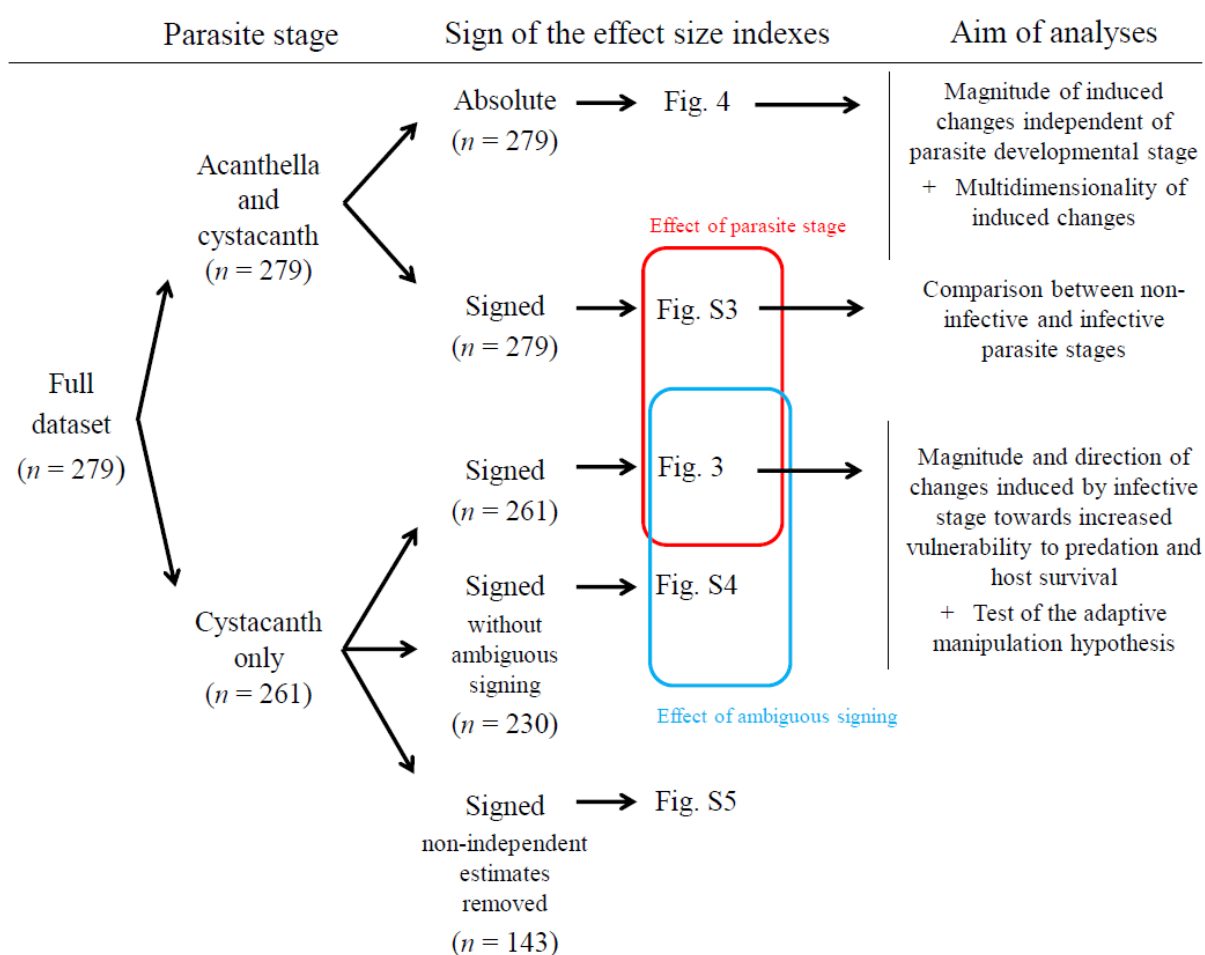


Table S2. Composition of the meta-analytic models in the complementary analysis run to explain variation in signed effect sizes (A) due to infection with acanthocephalans independent of parasite stage (incorporating effect size of both acanthella and cystacanth infection) and (B) due to cystacanth infection, excluding ambiguous traits (*cf.* Table 1). The corresponding deviance information criteria (DIC), and heterogeneity (I^2) arising from the random factors (parasite species, study and phylogeny) are provided. The best model, according to the lowest DIC, is shown in bold type.

A

Model	Moderators (fixed effects)	DIC	Heterogeneity I^2 (%) (random effects)		
			Parasite species	Study	Phylogeny
1	intercept only	250.96	10.41	29.33	19.11
2	category of traits	245.87	10.40	31.34	19.52
3	infection type	252.66	10.11	29.85	18.09
4	parasite stage	236.59	10.70	29.28	18.23
5	publication year	251.33	10.99	28.18	20.33
6	sample size	246.04	10.13	31.46	18.71
7	category of traits + parasite stage + sample size	226.33	9.40	32.90	18.11
8	category of traits + infection type + parasite stage + publication year + sample size	228.42	9.65	33.69	18.07

B

Model	Moderators (fixed effects)	DIC	Heterogeneity I^2 (%) (random effects)		
			Parasite species	Study	Phylogeny
1	intercept only	145.39	6.17	37.19	10.63
2	category of traits	133.49	6.74	40	12.54
3	infection type	146.55	6.18	36.58	11.47
5	publication year	146	6.24	37.59	10.50
6	sample size	136.19	6.18	39.68	10.43
7	category of traits + sample size	124.19	6.94	41.88	12.44
8	category of traits + infection type + publication year + sample size	126.04	6.95	42.22	13.08

Fig. S3. Parasite-induced alterations of mean trait value from the complementary analysis, incorporating all parasite developmental stages: forest plot with global meta-analytic mean of signed effect sizes (overall), and the meta-analytic mean for each moderator (categories and subcategories of traits, parasite maturity and type of infection). Positive effect sizes represent infection-induced alterations expected to increase trophic transmission, whereas negative effect sizes represent infection-induced alterations expected to decrease trophic transmission. *n*, sample size.

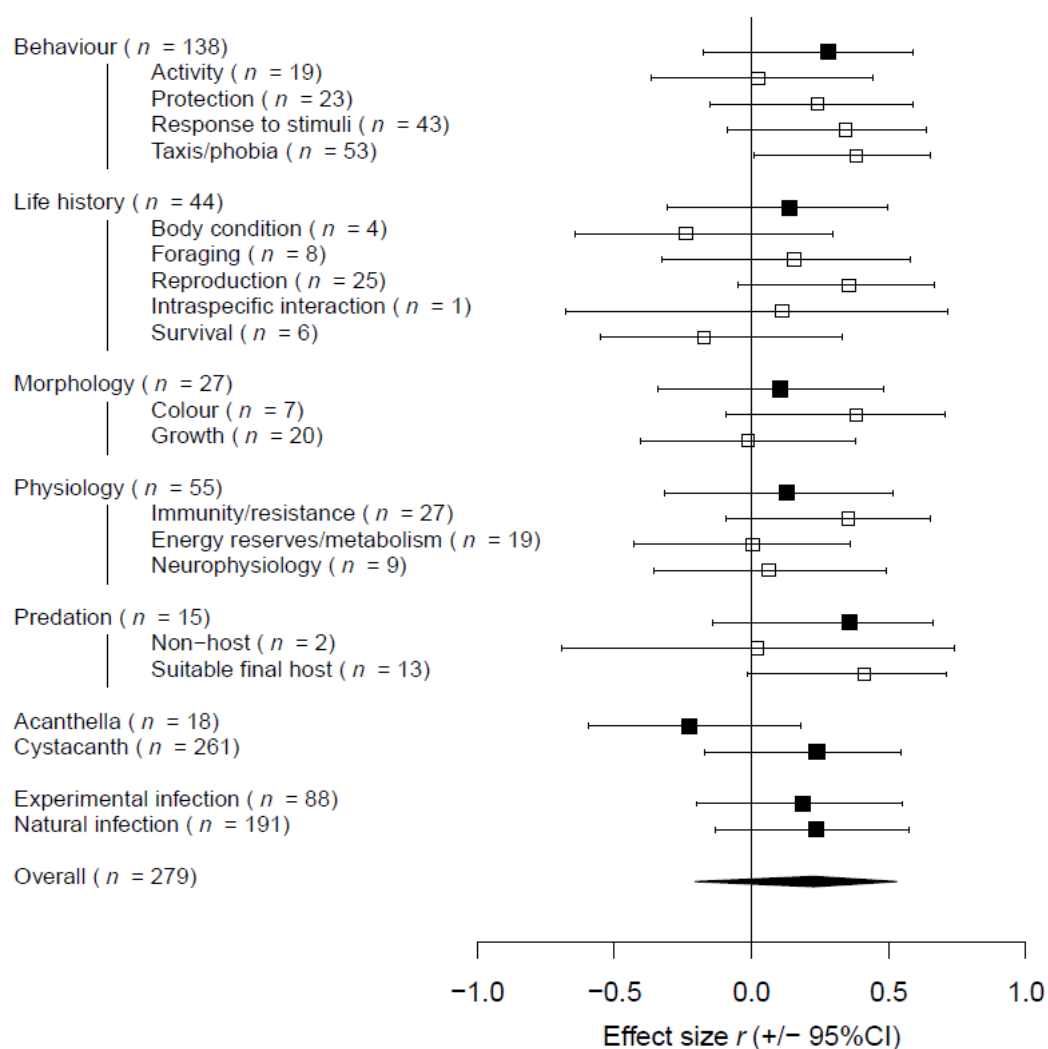


Fig. S4. Ambiguous traits: forest plot with global meta-analytic mean of signed effect sizes (overall), and the meta-analytic mean for each moderator (categories and subcategories of traits and type of infection). As the focus was on parasite transmission to final hosts, only effect size estimates for infection with cystacanths were included. The analysis was run after removing 31 ambiguous host traits with respect to their contribution to increased parasite transmission to final hosts [these traits were in the categories ‘activity’ (behaviour), ‘energy reserves/metabolism’ and ‘neurophysiology’ (both from physiology) and growth (morphology)]. *n*, sample size.

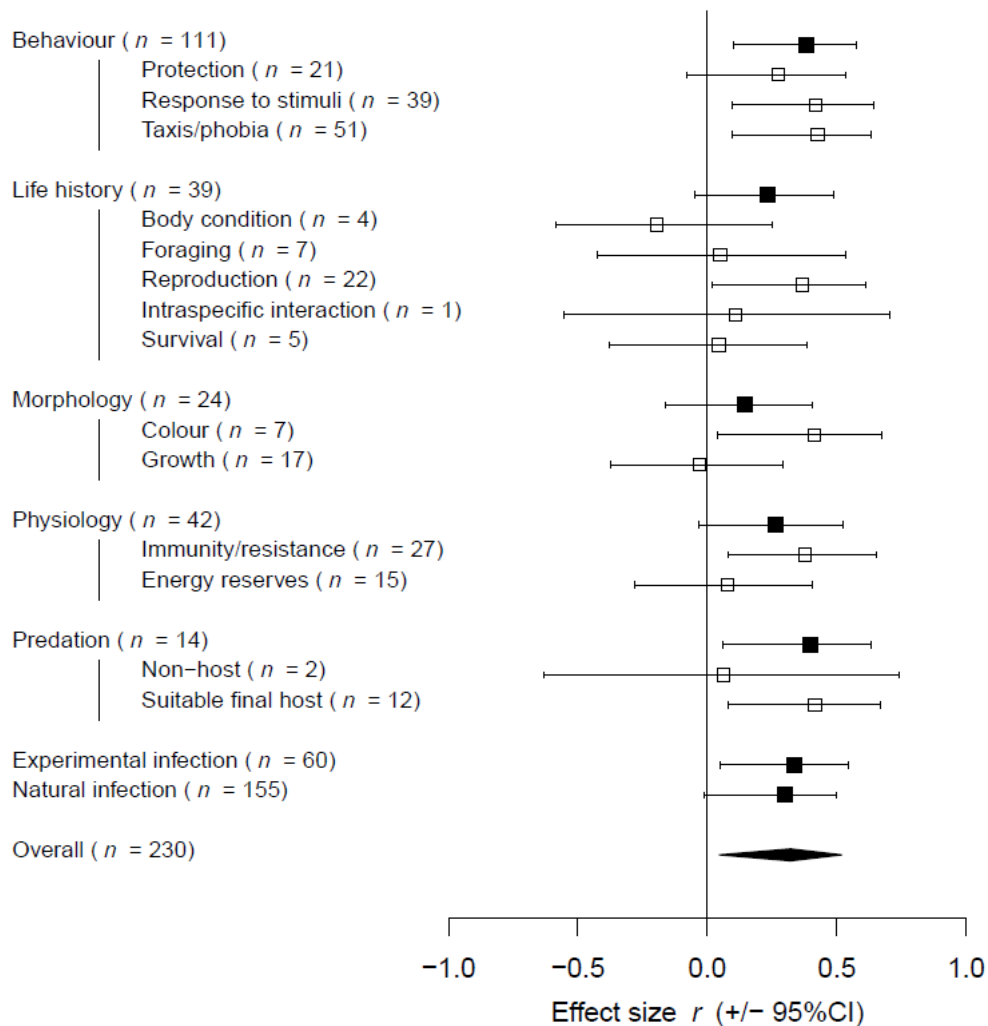


Fig. S5. Sensitivity analysis to account for the non-independence of effect sizes: forest plot with global meta-analytic mean of signed effect sizes (overall), and the meta-analytic mean for each moderator (categories of traits and type of infection). As the focus was on parasite transmission to final hosts, only effect size estimates of infection with cystacanths were included. The sensitivity analysis was performed by removing cases of pseudo-replication from the data set (mainly ‘shared measures’). *n*, sample size.

