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Review

After decades of stressor research in urban estuarine ecosystems the focus is still on single stressors: A systematic literature review and meta-analysis

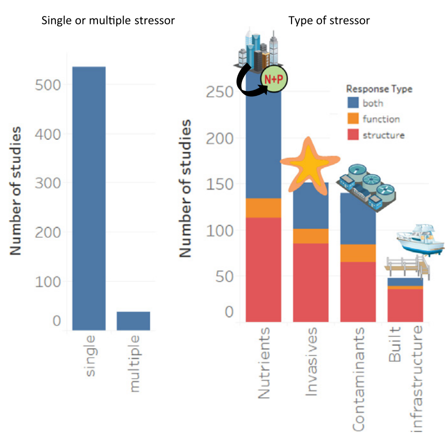
A.L. O'Brien [a,*], K.A. Dafforn [b,e], A.A. Chariton [c], E.L. Johnston [d], M. Mayer-Pinto [d,e]

[a] School of BioSciences, University of Melbourne, Parkville, Victoria 3010, Australia
[b] Department of Environmental Sciences, Macquarie University, NSW 2109, Australia
[c] Department of Biological Sciences, Macquarie University, NSW 2109, Australia
[d] Evolution and Ecology Research Centre, School of Biological, Earth and Environmental Sciences, University of New South Wales, Sydney, NSW 2052, Australia
[e] Sydney Institute of Marine Sciences, Mosman, NSW 2088, Australia

HIGHLIGHTS

- Multiple stressor interactions remain poorly understood in urban marine systems.
- Primary research has focused on nutrients and toxic contaminant interactions.
- Interactive effects of nutrients and toxic contaminants were not antagonistic.
- Structural endpoints decreased in response to single and multiple stressors.
- Functional endpoints responded in different ways to multiple stressors.

GRAPHICAL ABSTRACT



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ABSTRACT

Natural systems are threatened by a variety of anthropogenic stressors and so understanding the interactive threats posed by multiple stressors is essential. In this study we focused on urban stressors that are ubiquitous to urban estuarine systems worldwide: elevated nutrients, toxic chemical contaminants, built infrastructure and non-indigenous species (NIS). We investigated structural (abundance, diversity and species richness) and functional endpoints (productivity, primary production (chlorophyll-a) and metabolism) commonly used to determine responses to these selected stressors. Through a systematic review of global literature, we found 579 studies of our selected stressors; 93% measured responses to a single stressor, with few assessing the effects of multiple stressors (7%). Structural endpoints were commonly used to measure the effects of stressors (49% of the total 579 studies). Whereas, functional endpoints were rarely assessed alone (10%) but rather in combination with structural endpoints (41%). Elevated nutrients followed by NIS were the most studied single stressors (43% and 16% of the 541 single stressor studies), while elevated nutrients and toxic contaminants were overwhelmingly the most common stressor combination (79% of the 38 multiple stressor studies); with NIS and built infrastructure representing major gaps in multi-stressor research. In the meta-analysis, structural endpoints tended to decrease, while functional endpoints increased and/or decreased in response to different types of organisms or

* Corresponding author.
E-mail address: allyson@unimelb.edu.au (A.L. O'Brien).

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groups. We predicted an antagonistic effect of elevated nutrients and toxic contaminants based on the opposing enriching versus toxic effects of this stressor combination. Of note, biodiversity was the only endpoint that revealed such an antagonistic response. Our results highlight the continuing paucity of multiple stressor studies and provide evidence for opposing patterns in the responses to single and interacting stressors depending on the measured endpoint. The latter is of significant consequence to understanding relevant impacts of stressors in coastal monitoring and management.

Contents

1. Introduction

Urban estuaries provide key ecosystem services, with economic and social benefits, to the 3 billion people that live within 100 km of a coastline (IOC/UNESCO, 2011). However, the Anthropocene is placing increasing pressures on these environments, collectively resulting in the biological, chemical and physical degradation of coastal environments (Stauber et al., 2016b). While there are numerous studies examining the ecological implications of key stressors associated with anthropogenic activities, such as increased loading of nutrients and toxic contaminants in waterways (e.g. Clark et al., 2015; Lawes et al., 2017), for the most part these stressors have been examined in isolation, potentially providing an overly simplistic view of the true pressures facing coastal ecosystems (Dafforn et al., 2016). To date, meta-analyses have been useful in progressing this field of research by developing frameworks and definitions of multiple stressor interactions. For example, they may be additive where the effects of two or more stressors are simply summed up or they many interact causing antagonistic or synergistic effects (e.g. Crain et al., 2008; Strain et al., 2014; Griffen et al., 2016; Hale et al., 2017). Although relationships between multiple stressors and biodiversity or ecological status are reasonably well documented in some regions around the world (Andersen et al., 2015; Halpern et al., 2015; Ellis et al., 2017) there is still a gap in our understanding of the mechanisms underlying stressor interactions (Schafer and Piggott, 2018). Multiple stressor interactions are still rarely investigated beyond correlative relationships and interpretation remains difficult, often due to biological response that are highly variable (Chariton et al., 2016b; Dafforn et al., 2016; Berthelsen et al., 2018).

Historically, stressor studies in urban estuarine environments have measured biological responses with structural endpoints such as biodiversity, species richness and abundance, and compositional change of communities (e.g. Johnston et al., 2015; Chariton et al., 2016a). In comparison, endpoints that measure community function are less common (O'Brien et al., 2016) and are rarely interpreted in the context of the whole ecosystem, despite the clear effects of anthropogenic stressors on ecosystem functioning (Johnston et al., 2015; Strong et al., 2015). In some cases, ecological studies use community structure (e.g. presence of species tolerant to stress) to imply stress-induced impacts on ecosystem functioning (e.g. Vinebrooke et al., 2004). This ignores potential direct impacts of stressors on ecosystem functioning, which may occur independently of community structure (e.g. Mayer-Pinto et al., 2018b). We therefore need improved understanding of cause-effect relationships between single and multiple stressors and their biological effects (Schafer and Piggott, 2018), but also a clear understanding of what endpoints best represent these effects at the ecosystem level or scales that are relevant to management.

'Environmental filtering' can be used in decision-making to improve understanding and predictions of multiple stressor impacts (Schafer and Piggott, 2018; Van den Brink et al., this volume). Environmental filtering involves explicit decisions to select the ecosystem of concern, potential stressors, sensitive groups and endpoints likely to respond to different stressor combinations (Van den Brink et al., this volume). We applied this framework here to urban estuarine ecosystems ("harbours") and focused on four common urban stressors: nutrients, toxic contaminants (sensu Johnston et al., 2015), non-indigenous species (NIS) and built infrastructure. Here we define toxic contaminants as any metal, metalloid or synthetic organic compound (e.g. PAHS and pesticides) which is enriched at a concentration above 'natural' background concentrations for that specific area or organisms (Clark, 2001). When contaminants have a biological effect on organisms, assemblages and/or systems, they are called pollutants and, consequently, they cause pollution (GESAMP, 1980).

We used a systematic literature review to collect information on the types of functional (e.g. productivity, primary production (chlorophyll-a) and metabolism; see Table 1 for full list) and structural (e.g. abundance, diversity) endpoints used in stressor studies, taxonomic groups and the type of study (field experiment, survey, laboratory experiment, modelling). Using a meta-analysis approach, we then compared structural and functional endpoints measured in different communities for different stressor scenarios (single and multiple). We aimed to examine all stressor combinations, however, our quantitative analysis was restricted to nutrients and toxic contaminants, as this was the only combination of stressors that measured both structural and functional endpoints in a sufficient number of studies.

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Table 1
Search terms used to identify studies that assessed the effects of selected stressors using structural or functional endpoints.

Nutrients	Toxic contamination	Built infrastructure	Non-indigenous species
Nutrient* OR eutroph* OR sewage OR effluent	Contamina* OR pollut*	Pier OR jetty OR groyne OR seawall OR eco-engineering OR built infrastructure OR artificial structure ocean sprawl OR urbanisation OR hydro-morphology	Exotic OR non-indigenous OR pest OR invas*

Functional endpoints	Structural endpoints
Resilience OR tolerance OR resistance OR productivity OR production OR stability OR biomass OR photosynthesis OR respiration OR energy cycling OR food-web OR nutrient flux OR carbon cycle OR nitrogen cycle OR function*	Abund* OR biodiversity OR richness OR diversity

2. Methods

2.1. Literature review

We systematically reviewed studies that assessed the effects of one or more of the selected stressors (nutrients, toxic contaminants, built infrastructure, non-indigenous species (NIS) and measured a biological response in a coastal marine, harbour or estuarine system. We used ISI Web of Science Core Collection database to search for studies on each of the four stressors (Table 1). Search terms related to specific biological endpoints were also added to each search to keep the scope of the review manageable (Table 1). Functional measurements followed definitions in Johnston et al. (2015) and included rates of ecological processes, including fluxes of energy and matter within the system, such as carbon, water and mineral nutrients, or between trophic levels and the environment (e.g. productivity and decomposition, nutrient cycling), and their standing stocks. There were no restrictions on the date range. We limited the search to peer-reviewed journal articles that could be accessed through the Web of Science database to minimize any bias created by author background knowledge and search patterns.

A total of 2832 papers were returned and imported into a reference management tool (Endnote version X6.0.1). This included 990 papers on nutrients, 378 on contamination, 303 on built infrastructure, and 1161 on non-indigenous species. Duplicate papers were deleted. To be included in the review, papers needed to be a primary source of data that we could extract data from, therefore, reviews, discussions and method development papers were removed at this step (Fig. 1). We read all the relevant abstracts returned in the search and checked the stressors investigated in each study for duplication (e.g. the search terms used for toxic contaminants also identified some studies on nutrients, so these were checked and allocated appropriately in further analyses). We also found papers that were related to our selected stressors, but still outside the scope of the review. For example, studies on the impacts of aquaculture farms that can have effects related to nutrient enrichment were excluded as our 'nutrients' stressor category related only to nutrients associated with sewage and stormwater discharge. Only papers that measured the effect of the stressor(s) at the population or community level of biological organisation were included, which excluded studies on individuals (i.e. studies that used individual level endpoints, such as behaviour, physiology, cellular/molecular, genetics, bioaccumulation; see also Nõges et al., 2016). Although individual level endpoints are often used as early-warning signs of stress in ecotoxicology studies, we excluded these papers because this 'early-warning' link between individual and higher levels of biological organisation is rarely tested (O'Brien and Keough, 2014). In addition, by focusing on population and community level studies we collected information on endpoints that are most relevant to the higher levels of biological organisations that are of most interest to management, policy and the broader ideas of this paper (Beyer and Heinz, 2000; O'Brien, 2017). Collectively this resulted in 579 studies remaining from the original search.

Information recorded from each study ($n = 579$) included the country of study, type of stressor(s) (nutrients, contamination, built infrastructure, NIS), type of study (laboratory experiment, field experiment, survey/correlative study, or modelling) and the type of response measured (e.g. abundance, species richness, productivity, changes in trophic webs). The latter was then classified as structural or functional endpoints. The type of community or taxonomic groups were also recorded and categorized as algae and plants (including seagrass), microorganisms, plankton, invertebrates, fish, or 'community' if more than one of these groups were measured. We also recorded the number of stressors evaluated in the study and, if relevant, whether authors had tested for interactive effects.

2.2. Meta-analyses

There were 38 multiple stressors papers that assessed the impacts of two or more of the selected stressors. To be included in the meta-analysis, each paper needed to report the sample sizes, mean and standard deviation/standard error of the response variables or included figures from where these data could be extracted. Only papers with suitable replication and controls were included. In addition, the meta-analysis model required a measurement for each response variable in the presence of each stressor singularly (single) and in combination (multiple) and so this generally limited the selection to manipulative experiments. For example, surveys or correlative studies, which included BACI-style designs, were considered a multiple stressor study (i.e. included in the 38 multiple stressor studies), but could not be used in the meta-analysis as the stressor(s) were not manipulated and many in cases do not contain a true control – a treatment which only differed to the other treatments by its lack of contaminant (s) (Chariton et al., 2016a). Similarly, studies on NIS that did not manipulate the NIS, but measured it as a response variable were not used in the meta-analysis (e.g. indirect effects of NIS on a system). The remaining studies included 10 studies on the effects of nutrients and toxic contaminants, and two on the effects of nutrients and NIS (see supplementary data file). Since there were only two studies on nutrients and NIS, which is insufficient to draw any meaningful conclusions, we complied a data set for the meta-analysis using the 10 nutrients and toxic contaminants studies. The full list of multiple stressor studies and explanation of why they were included or excluded from the meta-analysis is in a supplementary data file. We extracted a total of 415 pairwise comparisons from the included studies. Each of these comparisons were the mean, standard deviation or standard error and samples size in the control/reference sites and 'treatment' (i.e. nutrients, toxic contaminants or nutrients and toxic contaminants). This information was recorded for each response variable reported in the paper and where information was only reported in figures the data was extracted using WebPlotDigitaliser (Version 4.1). If data were reported as a time series, only the data from the final sampling period was included in the meta-analysis (Strain et al., 2014). If data were reported on multiple species or at different sites in the same study, all information was recorded.

Meta-analyses were performed using r package metafor (Viechtbauer, 2010) in R gui 3.1.1 (R Core Team, 2016). As the data contained numerous zeros or negative values, effects sizes (the magnitude of the difference between control and treatment groups) were calculated using t Hedge's g standard mean difference (SMD) (Borenstein et al., 2009). To account for non-independence in the data, identifiers

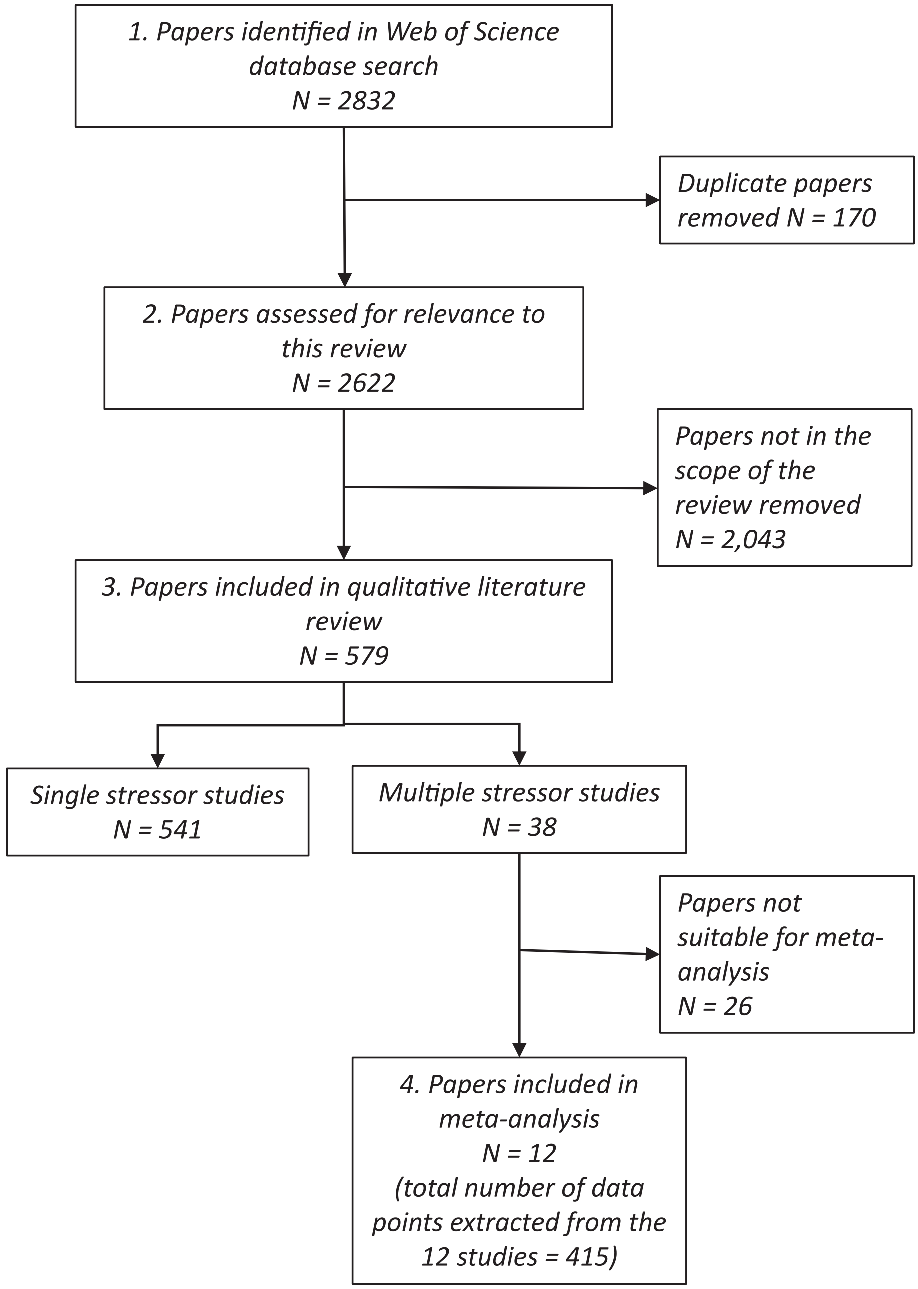

Fig. 1. Flow diagram showing the selection process for the literature review and meta-analysis. Step 1: Papers from the online database that met the initial search term criteria. Step 2: Papers assessed at the title and abstract level and, when necessary, the full-text. Review papers were removed at this step but kept separate for inclusion in our paper. Papers that investigated impacts of anthropogenic stressors but not one of our four selected stressors were excluded here. Step 3: The remaining papers were studies that assessed impacts of one of our four selected stressors – either singularly (single) or in combination (multiple). Data was recorded from all papers for the literature review analysis. Papers suitable for meta-analysis were identified at this step (i.e. papers that reported mean, standard deviation or standard error and samples). Step 4: Data for the meta-analysis were extracted for all response variables, but only for final time points (see Section 2.2 for further details on data extraction).

for "study" and "experiment" were included as random factors in the model, with experiment nested in study (Noble et al., 2017). Since all studies included in the meta-analyses were multiple treatment experiments, i.e. had one shared control for 2 or more treatments, we created a variance-covariance matrix to take into account correlated variances within study (Olkin and Gleser, 2009; Noble et al., 2017). Studies that show strong effects/impacts are more likely to be published rather than studies that have 'no effects' (Johnston et al., 2015). We then explored the drivers that we hypothesised would moderate the magnitude and direction of single and multiple stressors on biological responses.

3. Results and discussion

3.1. Literature review

Understanding interactions between multiple stressors is essential to advance management practices in the world's estuaries and coastal marine ecosystems (Halpern et al., 2007). In recent years, multiple stressor research has emerged as an independent discipline with frameworks and generalized models that have advanced this field of study (Ban et al., 2014; Piggott et al., 2015; Baird et al., 2016; Cote et al., 2016; Stock et al., 2018). However, we found the majority of studies in

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urban estuaries still investigate the effects of stressors in isolation (541 single stressor studies out the total 579 studies), with fewer than 7% of studies investigating the effects of stressors (nutrients, toxic contaminants, non-indigenous species or built infrastructure) in combination (38 multiple stressor studies). The largest number of papers was from Europe (35%) and North America (33%), with smaller contributions from Australia (7%), South America (5%) and China (4%). This follows a similar geographic distribution to other literature reviews on global aquatic ecosystems (Nõges et al., 2016; O'Brien et al., 2016). There have been several important contributions to this literature that map large-scale changes in multiple stressor effects (Nõges et al., 2016; Teichert et al., 2016), but the overall bias in the literature remains towards single stressor studies (Fig. 2; also shown by Nõges et al., 2016). We call for more empirical tests of multiple stressors using experiments to investigate mechanisms underlying cause-effect relationships.

3.2. Stressors

Nutrients were the most common anthropogenic stressor assessed in the literature; both in isolation (single, $n = 233$; Fig. 2a) and combination (multiple, $n = 36$; Fig. 2b). Thirty-six of thirty-eight multiple stressor studies assessed the effects of nutrients and one other stressor, with nutrients and toxic contaminants, such as metals, being the most common stressor combination ($n = 29$, Fig. 2b). This is similar to results in previous multiple stressor literature reviews, where nutrients and toxic stress the most common stressor combination estuaries (Nõges et al., 2016). Nutrient enrichment is a pervasive stressor in estuaries and urban marine environments worldwide and can be manipulated relatively easily (Stauber et al., 2016a; Birrer et al., 2017; Søndergaard et al., 2018). The ease with which both nutrients and other chemical stressors can be manipulated, particularly for field studies (Worm et al., 2000), and the global scale pervasiveness of eutrophication from urban and agricultural systems from diffuse and points sources may explain the proportionally larger number of nutrients and toxic contaminants studies (Stauber et al., 2016b).

Effects of NIS on urban estuarine biological populations and communities were commonly studied as a single stressor ($n = 86$, Fig. 2a). Multiple stressor studies that included NIS were: nutrients and NIS (5 studies); toxic contaminants and NIS ($n = 1$); built infrastructure and NIS ($n = 1$); and nutrients, toxic contaminants and NIS ($n = 1$). Many studies on NIS found in the literature search were excluded in the analysis as they considered the NIS population as the response variable rather than a stressor per se. These studies usually investigated how other anthropogenic stressors affected native communities via changes in abundances of NIS. The studies that we included were only those that explicitly considered NIS as a stressor and measured the effects of NIS themselves on the native communities. As a result, there is still a limited understanding of the extent and magnitude of potential impacts of NIS on structural and functional components of communities, which could potentially be significant (Cote et al., 2016). Possible explanations for the comparatively few studies that explicitly test the of effects of NIS relate to difficulties in manipulating and handling NIS for experimental studies, which pose legal and ethical issues and can only be done after a habitat has been invaded (if at all).

Built infrastructure was the least represented stressor category in both single and multiple stressors studies (Fig. 2). This stressor encompasses a range of artificial structures: piers, jetties, seawalls, artificial reefs, groynes, floodgates, drains and pipelines, as well as structures that are offshore (e.g. oil and gas rigs and windfarms), but also it can be considered more broadly as shipping (including dredging), aquaculture or coastal protection (Duarte et al., 2013). Here, we considered only artificial structures as the relevant stressor. The impacts of built infrastructure can be assessed as direct effects in the presence or absence of the actual structures, but equally relevant as indirect effects via changes in water flow, sedimentation or light regimes. Following the scope of our review on coastal estuarine habitats, we excluded any infrastructure that is typically offshore (e.g. windfarms and oil/gas rigs) and found that studies in the 'built infrastructure' category targeting seawalls, marinas, breakwaters (e.g. Stevens et al., 2004; Oricchio et al., 2016; Loyal et al., 2017) and artificial reefs (e.g. Qiu et al., 2003) were located in ports and harbours. Surveys were used to test the impacts of built infrastructure on the biological populations and communities ($n = 36$ survey studies), with some field experiments ($n = 13$) but no laboratory or modelling studies (Fig. 2). It is possible that studies investigating the indirect effects (i.e. water flow or hydrology, sedimentation or light regimes) associated with built infrastructure may not have been captured in our searches, which may partly explain the low representation in this review. In addition, given the growing prevalence of built infrastructures around the globe (Strain et al., 2018), we emphasize that there is pressing need to more clearly articulate the definition of built infrastructure in individual studies, and also the development of guiding principles to assess impacts from this stressor category that capture the complexity of the stressor-response relationships.

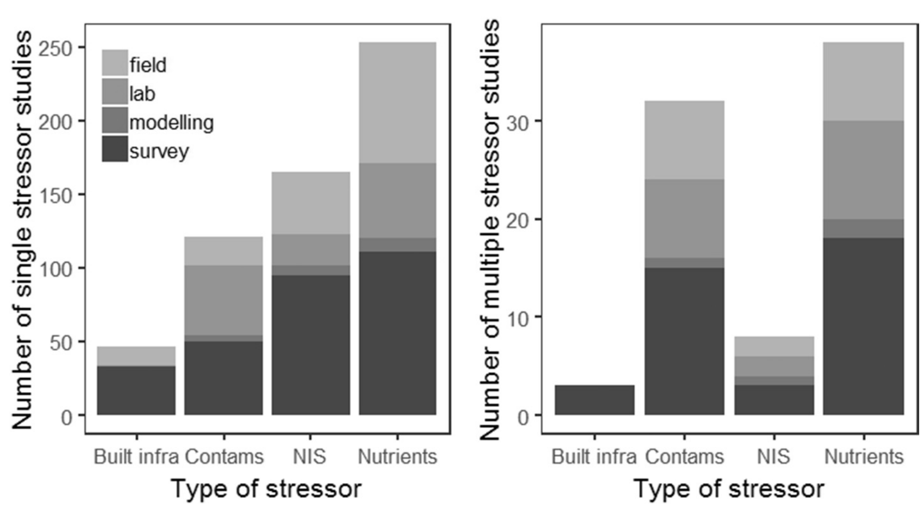

Fig. 2. Number of (a) **single** stressor studies and (b) **multiple** stressor studies that assessed the impact of built infrastructure (Built infra) toxic contaminants (Contams), NIS, or nutrients grouped depending on type of study (field experiment, laboratory experiment, modelling or correlative survey).

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3.3. Endpoints and taxonomic groups

Ecosystem functioning links to many services upon which humans rely (Turner et al., 2015). Yet, most studies on the effects of anthropogenic stressors at ecosystem scales are still strongly focused on changes to the structural components of communities, such as number of species and their abundance. Almost 50% of the reviewed studies here assessed effects of stressors using structural endpoints ($n = 277$), such as abundance, diversity and species richness (black bars in Fig. 3), while 10% of studies used functional endpoints ($n = 56$), such as productivity, primary production (chlorophyll-a) and metabolism (dark grey bars in Fig. 3). 41% of studies used both types of endpoints to measure biological responses to stress ($n = 235$), which included both structural and functional endpoints (light grey bars in Fig. 3). The use of the different endpoint categories was relatively consistent across different stressor categories for both single and multiple stressor studies (Fig. 3), except for the absence of multiple stressor studies that solely used functional endpoints in the NIS and built infrastructure stressor categories (Fig. 3).

The majority of studies that assessed structure were on macro-communities, including invertebrates and fish (Fig. 4). Other taxonomic groups were represented in studies that considered both structure and function, notably, algae/plants and plankton in single stressor studies (Fig. 4a) and microorganisms and plankton in multiple stressors studies (Fig. 4b). We expect that this reflects the objectives of many of these studies that aimed to investigate the impacts of anthropogenic stressors (single or multiple) at the habitat and ecosystem scale using a range of endpoints and taxonomic groups (also see Nõges et al., 2016).

Microorganisms and plankton are responsible for many of the fundamental ecosystem processes, such as primary productivity, respiration, and metabolism (Peter and James, 2000; Staehr et al., 2012), and so we expected to find responses in functional endpoints measured using these taxonomic groups. Instead, invertebrates were the group most commonly used in studies that measured functional endpoints (44% out of 55 single stressor studies: Fig. 4a). There were only two multiple stressors studies that measured functional endpoints, one study was on invertebrates and other on plankton (Fig. 4b). Undoubtedly, the relationship between biodiversity and functioning is complex (Hooper et al., 2005; Duffy, 2009; Strong et al., 2015). For example, the magnitude and extent of impacts of anthropogenic stressors depend not only on the type of species being affected/lost (e.g. McMahon et al., 2012; Mayer-Pinto et al., 2018b), but also of possible compensatory mechanisms occurring in the system where multiple components may absorb the effects (e.g. Ghedini et al., 2015).

Interestingly, the proportion of studies that measured multiple taxonomic and/or functional groups (hereafter referred to as whole communities) was still relatively small in both the single (13% of 579 studies) and multiple (8% of 38 studies) stressors studies. Studies across multiple taxonomic groups (e.g. bacterial, planktonic and macro-communities) are crucial to understand potential compensatory or synergetic responses of systems and not usually represented in biotic indices or biological trait analyses (e.g. Berthelsen et al., 2018). Negative effects of stressors on consumers, for instance, can have positive effects on primary producers, offsetting therefore potential impacts of the stressors themselves on primary productivity. Similarly, the higher turnover of bacterial communities might compensate for some of the effects caused by stressors on macro-communities, with important implications for the resilience of systems. Johnston et al. (2015) found studies that assessed multiple taxonomic groups within an entire community were more likely to find no effects of toxic contaminants than studies analyzing only a single functional/taxonomic group. Here, we found studies focused on particular taxonomic groups reflecting the study habitat types (e.g. soft sediment versus reef or water column), rather than having a more holistic approach, involving multiple trophic groups. For example, macro-invertebrates are commonly studied in environmental monitoring studies in soft sediment habitats (Berthelsen et al., 2018) and, and therefore tend to be the focus of studies in such habitats rather than microbial communities, for instance (but see Sun et al., 2012). We emphasize therefore, the importance of a more holistic view of urban systems, with studies that assess potential impacts of stressors on multiple trophic groups, preferentially, among different biological realms (i.e. microbes and macro-communities)(Lawes et al., 2017). Recent advances in molecular ecology, such as environmental DNA metabarcoding and RNA in metatranscriptomics, has made it easier and relatively simple to obtain whole community data including function through gene expression (Bohmann et al., 2014; Lawes et al., 2017; Sutcliffe et al., 2017; Birrer et al., 2018b; Taberlet et al., 2018). Given the rapid growth in this field (Dafforn et al., 2016; Birrer et al., 2017; Jarman et al., 2018), we anticipate that the whole community endpoints including structural and functional endpoints will be increasingly used in aquatic stressor research (e.g. Birrer et al., 2018a; Graham et al., 2018; Sutcliffe et al., 2018).

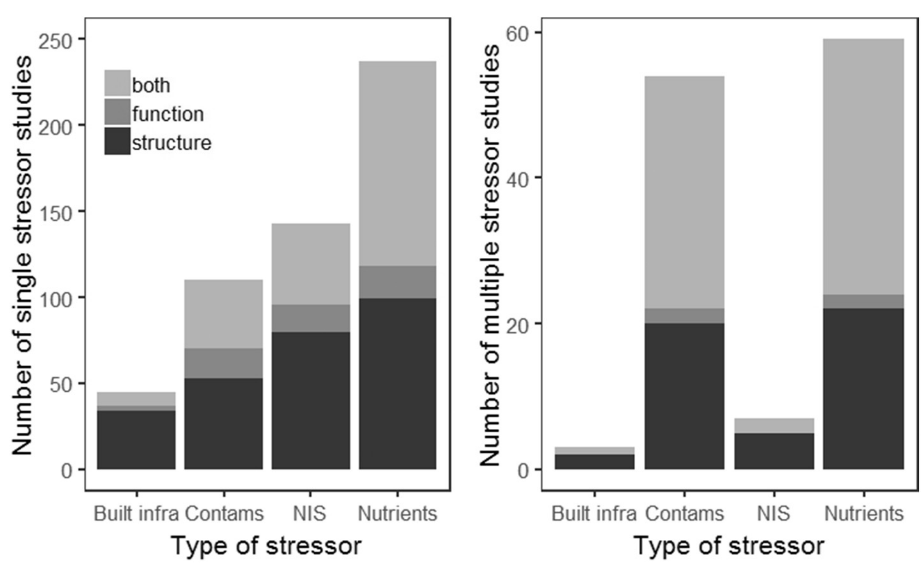

Fig. 3. Number of (a) **single** stressor studies and (b) **multiple** stressor studies that assessed the impact of built infrastructure, toxic contaminants, NIS, or nutrients using different endpoints (structural, functional or a combination both structure and function).

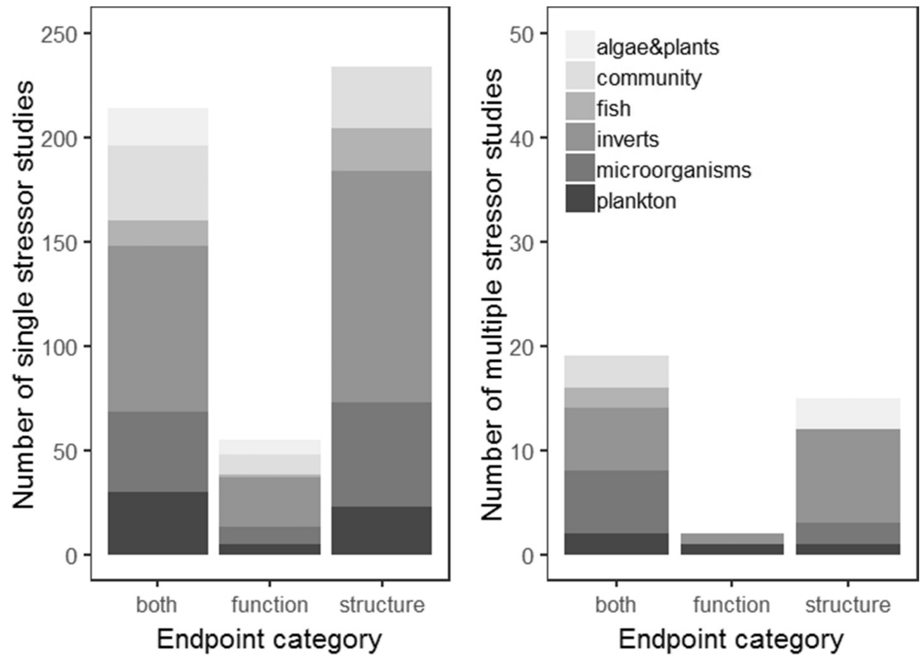

Fig. 4. Number of (a) **single** stressor studies and (b) **multiple** stressor studies that assessed the impacts of our selected anthropogenic stressors using structure and function ('both'), functional or structural endpoints across the different taxonomic groups (algae & plants, communities – defined as multiple taxonomic and/or functional groups, fish, invertebrates, microorganisms and plankton). See methods for further details.

3.4. Meta-analysis: nutrients and toxic contaminants

At very high levels of nutrient enrichment, coastal environments may become devoid of life, but, at moderate levels, productivity and biodiversity metrics such as species richness can be higher than background levels (Morris and Keough, 2003; Posey et al., 2006; Clark et al., 2015). These more moderate conditions are generally favoured by opportunistic species ('r-selected' species; Chariton et al., 2011), and can lead to marked increases in total abundance, biomass and diversity (Snelgrove et al., 1997). However, this generally comes at the expense to the often more sensitive and larger organisms ('k-selected' species; Pearson and Rosenberg, 1978). In contrast, contamination from toxicants (e.g. metals, pesticides) often has a negative effect on biological communities, decreasing ecosystem functioning, species abundances and diversity (Piola and Johnston, 2008; Johnston and Roberts, 2009).

In the context of a multiple stressor framework, we predicted that the combined effects of nutrients and toxic contaminants would generally be opposing or 'antagonistic', for example as shown by Lawes et al. (2017). However, we expected that this pattern would be influenced by factors such as the type of endpoint measured (structural or functional), taxonomic group and/or biological level of organisation, based on what we know about the complexity of urban estuarine ecosystems (Johnston and Roberts, 2009; Sun et al., 2012; O'Brien and Keough, 2014; Chariton et al., 2016b). The meta-analysis did not reveal strong differences between single and multiple stressors when broad endpoint categories, i.e. structure and function, were considered (Fig. 5). The combined effects of nutrients and toxic contaminants (multiple

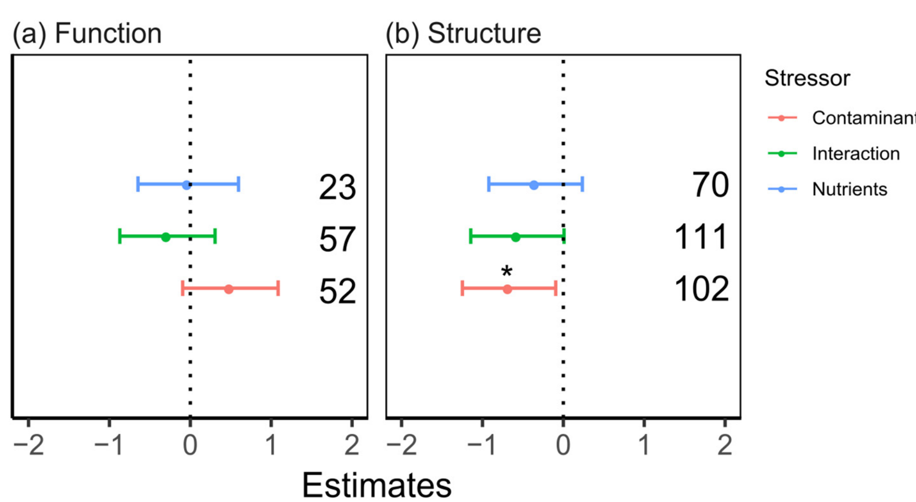

Fig. 5. Model estimates of effect sizes and confidence intervals (horizontal arms) from meta-analyses models of the functional and structural responses with stressors (i.e. toxic contaminants, nutrients and the interaction of both) as moderators. Numbers on the right as the number of data points from which estimates were calculated. Asterisks represent estimates that were significantly different from zero.

stressors) on structural (mean effect = −0.563 ± 0.294 (SE), p-value = 0.054) and functional endpoints (mean effect = −0.283 ± 0.300 (SE), p-value = 0.346) were negative with only structural endpoints significantly different from zero (Fig. 4). The effects of these stressors in isolation, as single stressors, were mostly similar to the magnitude and direction of multiple stressor effects for both structural (mean effect $_{nutrients}$ = −0.343 ± 0.295; p-value = 0.245, mean effect$_{contaminants}$ = −0.671 ± 0.294; p-value = 0.023) and functional endpoints (mean effect$_{nutrients}$ = −0.025 ± 0.317; p-value = 0.936, mean effect$_{contaminants}$ = 0.496 ± 0.301, p-value = 0.0996). Although these results do not strongly align with the antagonistic effects of nutrients and toxic contaminants demonstrated by (Lawes et al., 2017), it is possible that this more accurately reflects what is occurring and the complexity of disentangling cause-effect relationship. Responses to stressors are complex and vary depending the different stressor strengths and combinations, underlying mechanisms, individual and population level responses and trophic interactions (see Cote et al., 2016). In addition, these findings may also be attributed to the insensitivity of univariate metrics commonly used biological communities, such as diversity and richness, which have been criticised for their inability to detect anthropogenically induced effects even in cases where obvious changes in biological composition have occurred (Chariton et al., 2016a).

Chlorophyll a, used as a as a proxy for primary production, and metabolism tended to increase in response to stress, irrespective of the type of stressor or combination (Fig. 6; Table S1). However, these patterns were not strong, with wide confidence intervals and mean effect sizes that were not statistically different from zero (Fig. 6a & c). The possible mechanisms underlying these relationships are unclear, but would be an important interaction to explore further using in situ manipulative experiments.

In many aquatic systems, including those in temperate Australia, it is generally accepted that there is a predictive positive linear relationship between nutrients and chlorophyll a (ANZECC, 2000). However, as reflected in our findings, deviations from this trend do occur. For example, Sun et al. (2011) found no direct linear relationship between nutrients and chlorophyll a over a twenty-year period in Qingdao's Jiaozhoa River. In contrast, concentrations of chlorophyll a appeared to level off, with suggestions that phytoplankton may have been limited by other nutrients, such as silicate. A study on south-east Queensland estuaries

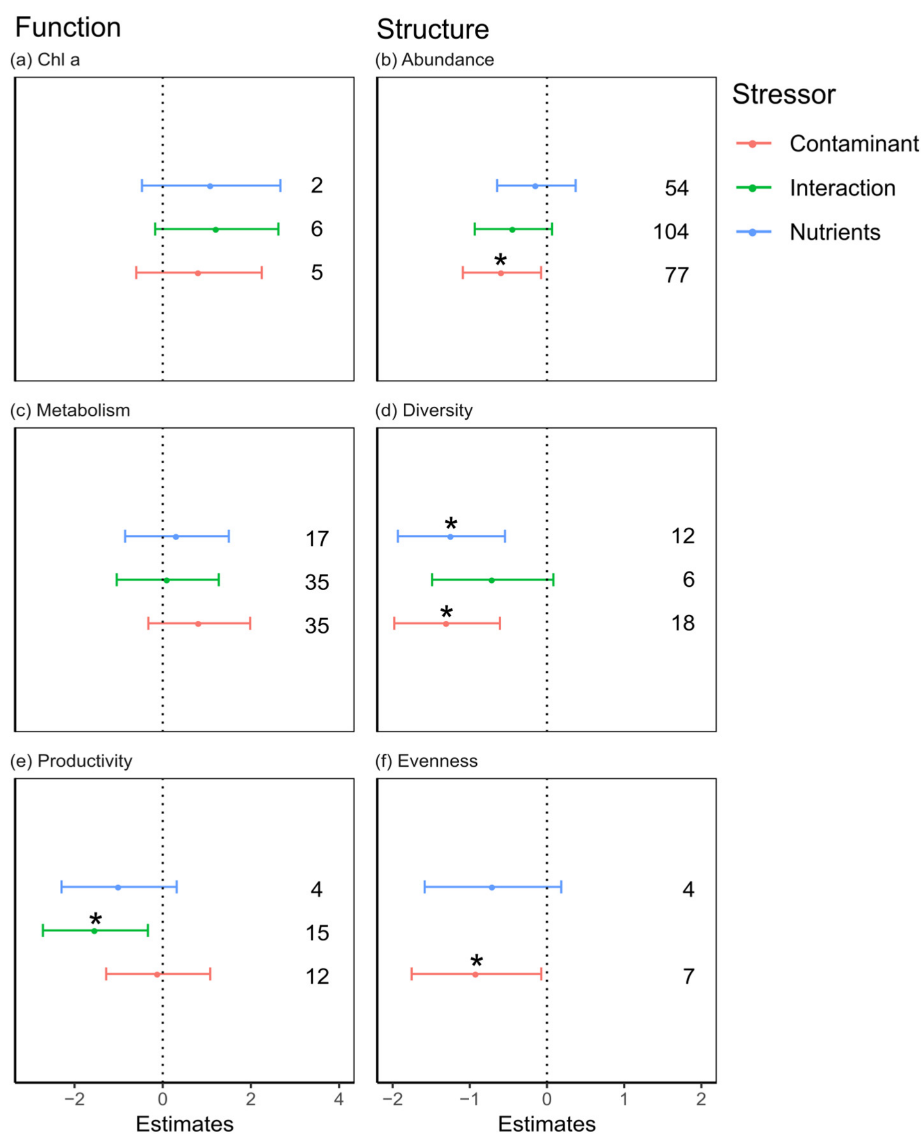

Fig. 6. Model estimates of effect sizes and confidence intervals from meta-analyses models of the different functional and structural endpoints with stressors (i.e. toxic contaminants, nutrients and the interaction of both) as moderators. Numbers on the right are the number of data points from which estimates were calculated. Asterisks represent estimates that were significantly different from zero. Interaction term for evenness was omitted from (f) as sample was one.

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further supports these findings, emphasising the challenges in predicting nutrient driven responses in chlorophyll *a* (Graham et al., 2018).

The opposite pattern was found for productivity where we found negative effects of both types of stressors and combinations (Fig. 6e). The mean effect of increased nutrients combined with toxic contaminants (i.e. interaction) was even greater, with a statistically significant negative effect, indicating a possible additive interactive effect of this stressor combination on productivity. While discharges of toxic contaminants into waterways are regulated in many countries around the world through licensing, nutrients and toxic contaminants continue to be are introduced from point and non-point sources during stormwater events (Birch and Lee, 2018). Our results suggest that the combination of nutrients and toxic contaminants will have strong, negative impacts on the productivity of harbours and urban coastal environments (as suggested by Birrer et al., 2018b), rather than having antagonistic effects (e.g. Lawes et al., 2017), dependant on the concentrations. Therefore, management should focus on regulation and remediation of further stormwater inputs (Sutherland et al., 2017).

Overall, structural endpoints (diversity, abundance, evenness) tended to decrease when exposed to single or multiple stressors (Fig. 6, Table S1). Diversity (e.g. Shannon's diversity index or number of species/taxa) was the only endpoint category that suggested an antagonistic interactive effect (Crain et al., 2008), where the effects of the single stressors (mean $\text{effect}_{\text{nutrients}} = -1.238 \pm 0.354$, p-value $= 0.001$, mean $\text{effect}_{\text{contaminants}} = -1.295 \pm 0.349$, p-value < 0.001) were greater than the combination of stressors (mean $\text{effect}_{\text{interaction}} = -0.703 \pm 0.401$, p-value $= 0.080$; Table S1). This is different to the pattern we found with productivity, where the interactive effect was greater than the effect of the single stressors (Fig. 6d). The differences between functional and structural responses to stressor combinations (single or multiple) highlights the importance of assessing other response variables in addition to the more traditional ones, such as diversity and number of species, which can mask or, even maximise, many deleterious effects

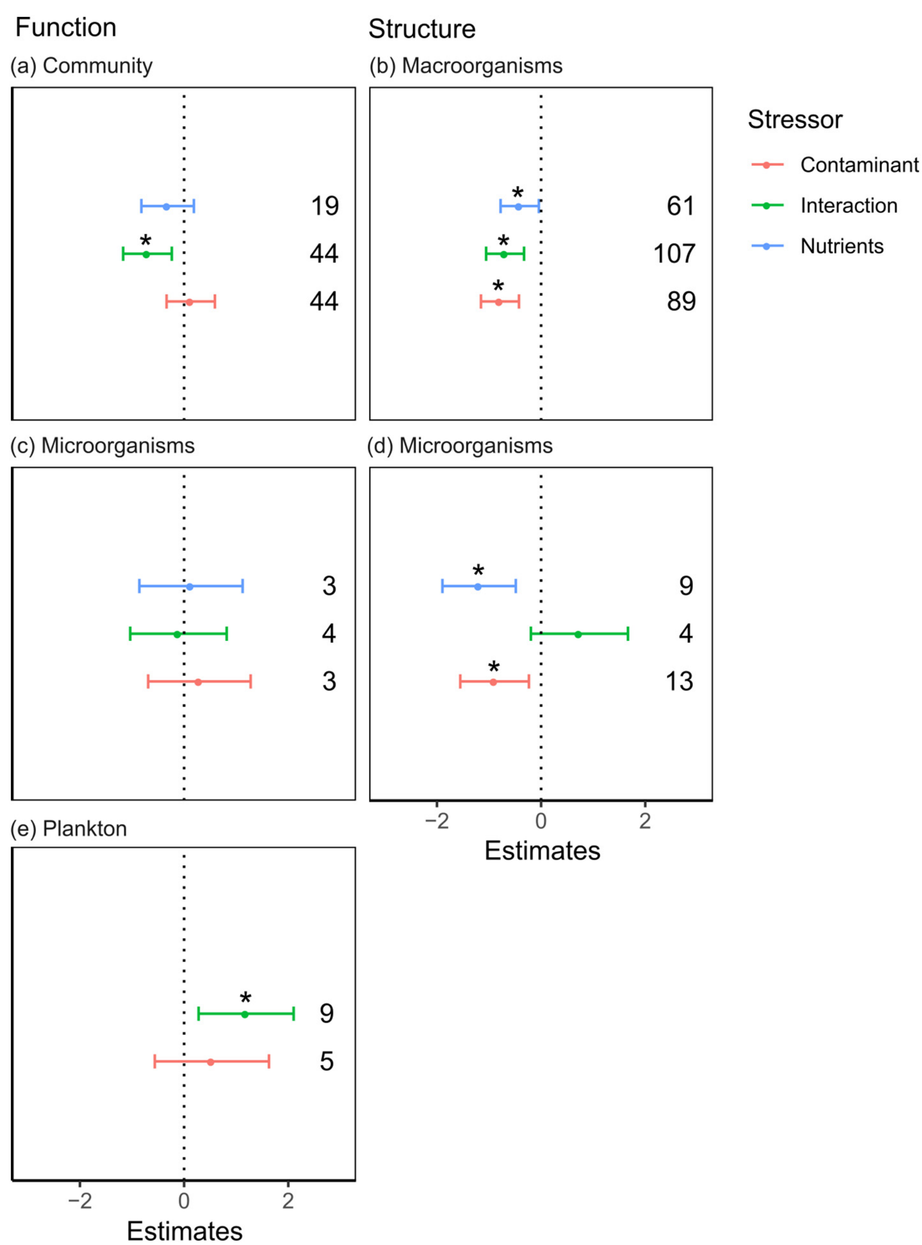

Fig. 7. Model estimates of effect sizes and confidence intervals from meta-analyses models with type of variable (i.e. structural or functional responses), stressors (i.e. toxic contaminants, nutrients and the interaction of both) and 'organisms' (e.g. micro or macro-organisms or the whole community) as moderators. Numbers on the right as the number of data points from which estimates were calculated. Asterisks represent estimates that were significantly different from zero.

of stressors on systems. A variety of new functional stressor endpoints are made increasingly available via modern molecular techniques (Birrer et al., 2018b) as well as new technological advances in ion-selective probes, and wet chemical and optical sensors (Pellerin et al., 2016).

We found that studies that measured 'community' responses to nutrients and contamination used functional endpoints such as primary productivity and nutrients fluxes in whole communities, mostly estuarine sediments (e.g. Petersen et al., 2009; Lohrer et al., 2012). These studies could not be separated into micro-or microorganism groupings and so were used as a separate moderator for the models using functional responses (Fig. 7a). At the community-level, contrary to the lack of effects observed when stressors were acting separately (i.e. single), the interactive effects of nutrients and toxic contaminants on functional responses were negative (Fig. 7a, Table 2S). At lower levels of taxonomic complexity (microorganisms and plankton) the functional responses were not as strong or even in the opposite direction (e.g. positive interactive term for plankton; Fig. 7e). Any robust conclusions about the functional responses by microorganisms and plankton groups were hindered by low sample sizes ($n < 10$; Fig. 7c & e), but functional responses at the community-level suggested an additive interactive effect that was greater than when the stressors acted separately. This pattern relates to the additive interactive effects on productivity (Fig. 7e), as many of the community-level studies used productivity endpoints (gross primary productivity) as a measure of ecosystem functioning.

Studies that used structural endpoints showed different response patterns depending on whether the target taxonomic groups were macro- or microorganisms. Abundances and diversity of micro-organisms decreased significantly in responses to single stressors of nutrients or toxic contaminants acting separately (Fig. 7d), but the interactive effect was positive, although not statistically significant from zero (Fig. 7d, Table 2S). This suggests an antagonistic interactive effect on the structure of microorganisms, consistent with what was found when diversity was tested as a separate moderator (Fig. 6d). In contrast, abundances and diversity of macro-organisms decreased when exposed to nutrients and toxic contaminants, acting separately or in combination (Fig. 7b). This highlights a potential incongruence between the interactive effects at different levels of biological organisation, with an antagonistic interactive effect on micro-organisms versus no discernible effect or difference between single and multiple stressors on macro-organisms. Mechanisms underlying the different responses may relate to greater functional redundancy in microbial communities or increases in abundance of opportunistic species in populations at higher levels of biological organisation that may be able to absorb stress, which potentially offsets the loss of other species that are vulnerable or rare when exposed to different stress regimes.

These results add to the current debate on interactive effects between stressors in estuaries, which have previously been dominated by additive interactions (Nõges et al., 2016; Teichert et al., 2016), but also documented as antagonistic in the context of ecological fish status (Teichert et al., 2016). Our results highlight a possible distinction between structural endpoints (e.g. diversity) that were characteristically antagonistic responses, compared to functional endpoints (e.g. productivity) that showed evidence of additive interactive effects of nutrients and toxic contaminants. Although robust conclusions from this meta-analysis are affected by low sample sizes for some of the model variations, there is evidence to suggest that effects of nutrients and toxic contaminants on functioning of urban estuaries at the community-level of biological organisation may be more severe than the effects on community structure, such as biodiversity and species abundances (at least when measured on macroinvertebrates which were the majority of test communities). In this case, assessing the effects of multiple stressors using structural endpoints only, may underestimate the severity of the effect on ecosystem function. Therefore, we recommend using both structural and functional endpoints when assessing ecosystem condition.

4. Conclusions

Predicting responses to multiple anthropogenic stressors continues to be a complex and challenging issue facing environmental science on a global scale (Schafer and Piggott, 2018). As a result, research has tended to focus on understanding responses to single stressors, despite calls for more empirical investigation of multiple stressors (Baird et al., 2016). Our literature review and meta-analysis highlight that after decades of stressor research, this practice continues and could be significantly hampering progress in management of multiply-stressed systems (e.g. Tett et al., 2013). The focus of our study was on stressors that act at the local or regional scale and can be specifically managed by waterway and coastal managers. In the future, it will be important to also consider interactions between other stressors that act at continental or global scales. We expect novel studies that manipulate a combination of stressors, particularly global scale variables related to climate change, such as pH, sea-level rise and frequency of storm events, will become the most relevant stressor combinations required to inform future coastal management (Molinos et al., 2016).

To have a more holistic and better understanding of impacts on urban systems, and consequently, better management of stressors, not only do we need to assess multiple stressors at any given time, but we need a better understanding of the link between structure and functional responses (Strong et al., 2015; Mayer-Pinto et al., 2018a). Our meta-analysis showed that structural endpoints generally decreased or had an antagonistic response to multiple stressors. In contrast, functional endpoints responded differentially with no interactive effects. Instead, we found an additive response to multiple stressors (e.g. productivity). It is probable that the mechanisms underlying the cause-effect relationships between multiple stressors and the different structural and functional endpoints are different and require different null models for predictions (Griffen et al., 2016; Schafer and Piggott, 2018). This is challenging from an ecological perspective as multiple stressor impacts are dependent on different endpoints and target taxonomic groups. For example, stressors may impact directly on ecosystem functioning, without changes in biodiversity or species abundances. In this we recommend careful consideration of the stressor (s) combinations and how they might interact with the exposed communities. Endpoints and taxonomic groups should therefore be targeted depending on the predicted severity of the impact and specific management objective or research questions (Dafforn et al., 2016).

Moving forward, the impacts of anthropogenic activities in urban estuaries needs to be considered in a multiple stressor framework (Griffen et al., 2016). The impacts of single stressors are evident from decades of research, but now we need to determine how these stressors are affecting urban estuaries in combination. Future meta-analysis studies using stressors other than nutrients and toxic contaminants would be an obvious next step, but as highlighted by our literature review, there are currently too few studies on the impacts of other stressors, including built infrastructure, non-indigenous species, to make this possible. Further research needs to focus on filling these knowledge gaps with an emphasis on carefully designed studies that include appropriate controls, temporal and spatial replication (Underwood, 1997; Gerstner et al., 2017) and the reporting of full data sets (i.e. non-significant results and errors or variability). This rigorous approach to design and reporting of multiple stressor research will improve our ability to quantitatively synthetize knowledge, develop predictive models and make an important contribution to how multiple stressors are managed in urban estuarine ecosystems.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2019.02.131.

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