Is It in the Stars? Exploring the Relationships between Species' Traits and Sea Star Wasting Disease

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Abstract

An explanation for variation in impacts of sea star wasting disease across asteroid species remains elusive. Although various traits have been suggested to play a potential role in sea star wasting susceptibility, currently we lack a thorough comparison that explores how life-history and natural history traits shape responses to mass mortality across diverse asteroid taxa. To explore how asteroid traits may relate to sea star wasting, using available data and recognizing the potential for biological correlations to be driven by phylogeny, we generated a supertree, tested traits for phylogenetic association, and evaluated associations between traits and sea star wasting impact. Our analyses show no evidence for a phylogenetic association with sea star wasting impact, but there does appear to be phylogenetic association for a subset of asteroid life-history traits, including diet, substrate, and reproductive season. We found no relationship between sea star wasting and developmental mode, diet, pelagic larval duration, or substrate but did find a relationship with minimum depth, reproductive season, and rugosity (or surface complexity). Species with the greatest sea star wasting impacts tend to have shallower minimum depth distributions, they tend to have their median reproductive period 1.5 months earlier, and they tend to have higher rugosities relative to species less affected by sea star wasting. Fully understanding sea star wasting remains challenging, in part because dramatic gaps still exist in our understanding of the basic biology and phylogeny of asteroids. Future studies would benefit from a more robust phylogenetic understanding of sea stars, as well as leveraging intra- and interspecific comparative transcriptomics and genomics to elucidate the molecular pathways responding to sea star wasting.

Introduction

Sea stars (Asteroidea) play essential ecological roles in diverse, economically important ecosystems; however, considerable knowledge gaps remain in our understanding of their evolutionary relationships, basic biology, and natural history. Consequently, we remain unaware of roles

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Abbreviations: MME, mass mortality event; MRP, matrix representation parsimony; PLD, pelagic larval duration; SSW, sea star wasting.

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that evolutionary (*e.g.*, Parker *et al.*, 2015) and ecological (*e.g.*, Garrett *et al.*, 2009; Chen and Zhou, 2015) diversity may have played in the geographically and taxonomically widespread mortality associated with a sea star wasting (SSW) outbreak widely reported as beginning in 2013 (Hewson *et al.*, 2014). Likewise, while many sources of largely disaggregated information are available for various asteroid species, we lack a synthetic framework that combines asteroid evolutionary relationships with information about their life and natural histories that may shape vulnerability to mass mortality.

To date, most exploration of factors possibly associated with the 2013 (or historical) SSW outbreak(s) have focused on causes extrinsic to the sea star—for example, population density (Miner *et al.*, 2018), pathogens (Hewson *et al.*, 2014), position in the intertidal (Menge *et al.*, 2016; Montecino-Latorre *et al.*, 2016), wave exposure (Bates *et al.*, 2009), salinity (Dungan *et al.*, 1982; Bates *et al.*, 2009), and water temperature (*e.g.*, Eckert *et al.*, 2000; Bates *et al.*, 2009; Staehli *et al.*, 2009; Eisenlord *et al.*, 2016; Kohl *et al.*, 2016; Harvell *et al.*, 2019). While there have been some tentative links established between SSW and a possible viral pathogen (Hewson *et al.*, 2014; Fuess *et al.*, 2015; Bucci *et al.*, 2017), these links are not considered definitive (Hewson *et al.*, 2018). By contrast, the role of factors intrinsic to sea stars has been understudied (Oulhen *et al.*, 2022). Yet understanding SSW's associations with life-history and natural history traits could help clarify whether and how the disease is linked to the extrinsic environment, whether abiotic or biotic. If there is an abiotic extrinsic influence (whether direct or mediated biotically), for example, we might predict that species' intrinsic trait similarity in habitat, phenotype, or endogenous cycles (*e.g.*, annual reproduction) may be a valuable predictor of SSW. If there is a trait-abiotic association, it does not exclude extrinsic biotic factors, including a potential pathogen: the abiotic environment may increase stress in the host, thereby increasing vulnerability to opportunistic pathogens (George *et al.*, 2014; Fey *et al.*, 2015). Alternatively, changing environmental conditions could be altering a pathogen's distribution or allowing for more proliferation, leading to more frequent interactions between the host and the infectious agent. Any of these scenarios may expose susceptibilities intrinsic to the sea star that are shared across closely related taxa, convergent in unrelated taxa, or unique to particular species.

Thus, here, we explore SSW severity and life-history traits within a phylogenetic context as an important first step in considering whether SSW severity is associated with evolutionary relatedness and/or life-history and natural history traits. We consider seven traits, reconstructed from data in the literature, for which we explore a relationship with SSW impact. (1) Developmental mode, for example, whether larvae are feeding or non-feeding, and (2) pelagic larval duration (PLD) have important implications for SSW epidemiology, if pathogenic. (3) Timing of peak reproductive season may be important because of differences in resource allocation during seasonally high SSW (which tends to increase toward the late summer; Montecino-Latorre *et al.*, 2016) or may be associated with changing temperature. We also tested whether a particular (4) diet or (5) substrate may play a possible role in SSW, through ingestion of or exposure to certain microbes or molecules or environmental conditions. Historical wasting events have implicated (6) depth as an important risk factor for wasting, with shallower depths resulting in more wasting due to salinity and/or temperature fluctuations (Dungan *et al.*, 1982). Finally, Aquino *et al.* (2021) found an association with wasting and higher (7) rugosity (*i.e.*, the surface complexity of the sea star that may have important consequences for the microbial community and gas exchange on the sea star surface). We synthesize these trait data in a phylogenetically informed manner to catalyze future efforts toward understanding the factors that influence vulnerability to SSW and demographic declines associated with SSW.

Materials and Methods

Sea star wasting impact assessment

Various studies have surveyed the impacts of SSW-driven mortality on various asteroid species. Without a standard approach for quantifying population declines in many species, we have opted to assign four categories of SSW impact—(1) no detected impact, (2) likely affected (limited quantitative data), (3) noticeable mortality, and (4) high mortality—based on published studies of documented declines (Montecino-Latorre *et al.*, 2016; Bucci *et al.*, 2017; Miner *et al.*, 2018; Harvell *et al.*, 2019; Hewson *et al.*, 2019; Jaffe *et al.*, 2019; Konar *et al.*, 2019; Hamilton *et al.*, 2021; M. N Dawson *et al.*, unpubl. data), assessment reports (University of California, Santa Cruz, 2018), and observations (Tables S1, S2, available online). Distinctions between these four categories largely follow consistent qualitative evaluations of these studies in rank order declines or proportion of wasting observations—that is, the relative mortality between species is reflected. The specific categories are broken down as follows: "no detected impact" means that the species was surveyed and no wasting observations or population declines were documented; "likely affected (limited quantitative data)" reflects species for which very few wasting observations were made or there was only a slight population decline during 2013–2015; "noticeable mortality" represents species for which there are more observations of wasting (relative to the "likely affected" group) and/or documented population declines; and "high mortality" reflects species for which there have been numerous observations made of wasting individuals and/or steep population declines (see Table S2 for a summary of qualitative results from SSW sources).

Life-history and natural history character data

We next conducted a literature search to collect life-history and natural history details for target asteroid species. These included depth, substrate, developmental mode, PLD, reproductive season, diet, rugosity (a measure of small-scale variation in surface height), and SSW impact (from above) (Table S3, available online). We also summarized the geographic distribution of species—using principal component analysis (PCA) in FactoMineR (Lê *et al.*, 2008) to reduce multidimensional data to a single linear dimension to facilitate coding for phylogenetic analyses—but because there was significant overlap in distributions and because taxa were drawn predominantly (but not totally) from one coastline, we did not analyze this trait for an association with wasting.

To code the diverse data types for phylogenetic analyses, we binned similar descriptive traits into categories: latitudinal distribution (five broad groups and nine more specific groups identified by the first PCA dimension), substrate (four groups: rock; soft sediments; rock, gravel, pebbles, cobbles; and rock and soft sediments), developmental mode (four groups: benthic lecithotrophs [*i.e.*, brooded], pelagic lecithotrophs, pelagic planktotrophs, and mixed benthic and pelagic lecithotrophs), PLD (three groups: no PLD, shorter [median <65 days], and longer [median ≥85 days]), reproductive season (two groups: primarily spring/summer and other times), diet (six groups: detritus, Porifera, Cnidaria, Mollusca, Echinodermata, and generalist [defined as consuming ≥4 phyla; we settled on this cutoff given that the literature identifies *Leptasterias* sp. as a generalist predator consuming three phyla plus detritus; the exception in our list is *Dermasterias imbricata*, which has been documented consuming five phyla but has a preference for anemones]), and SSW impact (as described in *Sea star wasting impact assessment*). Note that for traits with continuous data—depth (minimum, median, and maximum) and rugosity—we used raw values; but, given the high amount of missing data in estimates of PLD, rather than handling it as continuous, we assigned values to three broad categories that had distributional breaks between each. For reproductive season, we calculated the median numerical month of peak reproductive season. Depth was binned into categories to visualize on the phylogeny using the shallow end and deeper end of species' distributions. Shallowest bins—that is, the shallow end of the species' depth distribution—included 0–0.5 m, 0.5–8 m, 9–14 m, and >14 m; deepest bins included intertidal, subtidal to 20 m, 20–200 m (~epipelagic), 200–1000 m (~mesopelagic), and 1000–4000 m (~bathypelagic). When a specific trait could not be scored for a given species because of lack of data, it was categorized as missing data.

Analyses of phylogenetic association in character data

To consider phylogenetic associations in SSW impacts—as a first step for conducting correlations between SSW and various life-history and natural history traits—we first needed to generate a phylogeny for the species of interest. While a highly resolved phylogeny does not exist for the species known to be affected, we leveraged relevant and available datasets (*i.e.*, Janies *et al.*, 2011; Mah and Foltz, 2011a, b; Reich *et al.*, 2015; Linchangco *et al.*, 2017) that represent the necessary breadth, across all major superorders of Asteroidea, with sufficient depth to generate an initial working phylogenetic hypothesis for asteroids with previously reported SSW outcomes. Notably, species represented in asteroid phylogenetic studies are geographically biased by where asteroid systematists and biologists reside and study. This bias also likely accounts for these areas also being the best studied in terms of SSW, and there are significant gaps in understanding of the spatial and taxonomic prevalence of SSW (M. N Dawson *et al.*, unpubl. data). As a result, the pruned tree we use here is dominated by species with previously reported SSW outcomes.

From these studies, we selected all three molecular trees (differing in the assumptions of inference but using the same data) in Janies *et al.* (2011), the optimal topology reported by Linchangco *et al.* (2017), and the best trees reported by Reich *et al.* (2015) for inclusion in a supertree analysis. These trees were reduced to include only the asteroids and one ophiuroid outgroup. We also generated topologies based on data from Mah and Foltz (2011a, b), using their alignment (provided by the authors, generated using ClustalX [Larkin *et al.*, 2007] and GBLocks [Castresana, 2000]) of 183 taxa and 1084 characters—254 bp of the mitochondrial *12S* rDNA gene, 503 bp of the *16S* rDNA gene, and 327 bp of the nuclear early-stage histone *H3* gene. These aligned data were submitted to CIPRES (Miller *et al.*, 2010) as a sequential PHYLIP file for analysis by RAxML 7.2.0 (Stamatakis, 2006). The "RAxML-HPC2 on XSEDE . . . 31 parameter set" instance was used with default parameters unless different from Mah and Foltz (2011a, b). We specified the following options: (1) bootstrapping with 150 replicates, (2) a mixed/partitioned model with each gene region treated separately, (3) per-gene branch length optimization, and (4) the GTRGAMMA substitution model. A bootstrap majority rule consensus tree was then made using the CONSENSE software at CIPRES (Miller *et al.*, 2010) to include in supertree analyses.

Given the differential quality of data and taxonomic coverage available in the above set of trees, a supertree was created using the matrix representation parsimony (MRP) method (Baum and Ragan, 2004) in the phytools R package and implementing the parsimony ratchet method (Nixon, 1999) to search for the preferred tree. The tree from Linchangco *et al.* (2017) utilized a large amount of transcriptome data and was considered the most robust phylogeny but lacks key taxa of interest. The Linchangco *et al.* (2017) tree was therefore weighted by duplicating this tree in our MRP analysis to account for this higher quality of data (as described in Garamszegi, 2014). We explored two alternative tree-weighting schemes to the one described above by (1) increasing individual tree representation to equally weight each of the four papers and (2) equally weighting each tree (Table S4, available online; see also supplementary methods, available online). We evaluated the impact of the different weighting schemes on tree topology and phylogenetic correlation in SSW (Figs. S1–S3, available online).

Having evaluated phylogenetic correlation in SSW and life-history and natural history traits, using the full tree, we generated a reduced tree for analyses of continuous data and for visualization. We filtered the supertree by using Dendroscope (Huson *et al.*, 2007) to include taxa primarily from the northeast Pacific and northwest Atlantic (where the primary observations of SSW have been made) and for which data on SSW impact were available (see *Sea star wasting impact assessment*, below). In the filtered tree we substituted (by replacing) or added (by grafting) taxa of interest that were assumed congeners: substituting *Astropecten articulatus* and *Astropecten polyacanthus* with *Astropecten armatus* and *Astropecten californicus*; *Heliaster helianthoides* with *Heliaster kubiniji*, *Hippasteria spinosa* with *Hippasteria phrygiana*; *Leptychaster propinquus* with *Leptychaster pacificus*, *Linckia nodosa* with *Linckia columbiae* and adding *Henricia pumila* as sister to *Henricia* sp., and *Pteraster militaris* as sister to *Pteraster tesselatus* (Table S1, available online).

We used two different approaches to explore phylogenetic associations in trait data. (1) We analyzed continuous traits for which we extracted the first dimension of principal component and continuous traits—latitude (dimension 1), median month of peak reproductive season, depth (minimum, maximum, and median), and rugosity (the ratio of the actual 3D surface area from X-ray micro-computed tomography data and 2D surface area of a standard 1-cm segment of arm from Aquino *et al.*, 2021)—using Pagel's λ in PhyloSignal v1.3 (Keck *et al.*, 2016) in R v.4.0.3 (R Core Team, 2020) and assigned significance if $P < 0.05$. Data were plotted using PhyloSignal after being centered (by subtracting the mean of the trait from each value) and scaled (by dividing the centered values by the standard deviation). (2) We analyzed categorical trait—substrate, diet, reproductive season, PLD, developmental mode, latitude (five groups and nine groups), and SSW—using Mesquite v3.5 (Maddison and Maddison, 2018) to compare whether the steps required to explain the distribution of character states differed from states randomly assigned to the tips of the same tree (for 999 permutations) and assigned significance if the number of steps fell below the fifth percentile of the distribution. Because we conducted multiple tests, we did a Benjamini-Hochberg adjustment. The sensitivity of a phylogenetic correlation in SSW was evaluated using three different tree-weighting schemes (supplementary material, available online; Table S4, available online).

Sea star wasting-trait associations

After testing for the influence of phylogeny on the distributions of traits on the tree, we used several approaches to test for associations between specific traits and SSW impacts. For categorical traits (developmental mode, diet, and substrate) we used a chi-squared test to test the observed combinations of character states for each trait + SSW against the randomized distribution of possible pairs (*e.g.*, for developmental mode and SSW: pelagic lecithotrophs + SSW high mortality, pelagic lecithotrophs + SSW noticeable mortality, pelagic planktotrophs + SSW high mortality, *etc.*). For PLD-SSW comparisons, we categorized species into two groups based on SSW status (higher mortality: high mortality + noticeable mortality; lower mortality: no detected impact + likely affected) and three groups based on PLD (no PLD; shorter: median <65 days; longer: median ≥85 days), then we used a chi-squared test to test whether SSW status and PLD character state pairs were different from those expected by random chance. For latitude, both the substantial overlap in species' distributions and the fact that species in this study came from primarily (but not totally) a single coastline precluded a balanced test of an association with SSW impact.

For continuous traits—maximum depth, minimum depth, and rugosity—we split the traits into high and low bins: maximum depth (shallow: ≤100 m; deep: ≥250 m), minimum depth (shallow: ≤0.5 m; deep: ≥5 m), and rugosity (low: ≤0.40; high: ≥0.42). We used the same binary binning for SSW as above. For each trait we used a chi-squared test to test whether SSW-trait pairs were different from that expected by random chance. For reproductive season-SSW comparisons, we separated species into two groups based on SSW impact status: (1) higher mortality (high mortality + noticeable mortality species) and (2) lower mortality (no detected impact + likely affected), then we used a *t* test to compare the mean peak reproductive month between the two groups. Significance was assessed at $P < 0.05$ after correcting for multiple tests, using a Benjamini-Hochberg adjustment.

Results

Life-history and natural history characters and phylogenetic association

The full supertree (Fig. S1a, available online), which represents most major Asteroidea clades, was subsequently filtered to 31 asteroids identified in the sources in *Sea star wasting impact assessment* (Fig. 1; sea star photo credit is summarized in Table S5, available online). Consequently, placement of some taxa may be precarious if they were represented in only a single tree (*i.e.*, *Linckia columbiae*) and may result in sister taxa being separated because it was not represented together in more than one tree (*i.e.*, *Pycnopodia helianthoides* + *Rathbunaster californicus*; Fig. 1). Species' presence in the original source trees is summarized in Table S1 (available online) for all species in Figure 1. The sensitivity analyses using the three different weighting schemes (Table S4, available online) generated largely but not completely congruent supertree topologies (Fig. S1; Fig. S2, available online); the small differences did not impact the outcome of phylogenetic correlation analyses of SSW impact (Fig. S3, available online). Additionally, because we used taxon names as they appeared in their original publication for the full tree (Fig. S1, available online), we

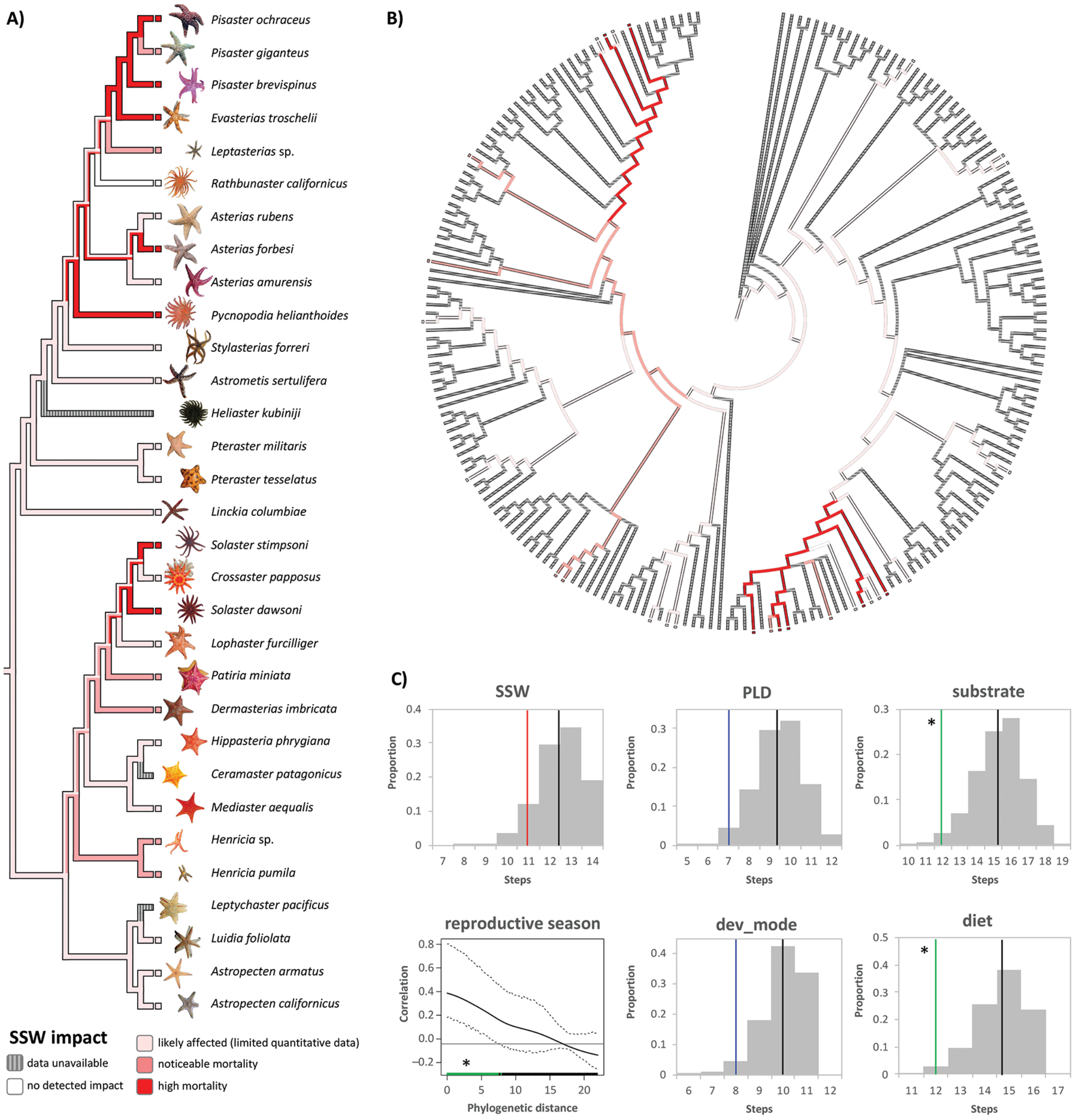

Figure 1. Asteroid cladogram constructed using the matrix representation parsimony (MRP) method integrating trees from previously published phylogenetic studies (Janies *et al.*, 2011; Mah and Foltz, 2011a, b; Reich *et al.*, 2015; Linchangco *et al.*, 2017). (A) We filtered species to include only those for which we have sea star wasting (SSW) data or that were taxa of interest. (B) The full supertree represents the 75% consensus tree of the 10 topologies generated using the up Linchangco 2x weighting scheme. The MRP method does not account for branch support values; therefore, none are shown. The color at the tips indicates relative SSW impact; gray barred shading indicates species for which no recent wasting observations were available. (C) For categorical traits—SSW, pelagic larval duration (PLD), substrate, developmental mode (dev_mode), and diet—the gray histograms show the number of steps required to explain the distribution of character states if they were randomly distributed on the phylogeny (calculated for 999 trees). The black line in each plot represents the mean number of steps averaged over all 999 runs. The colored lines represent the number of steps based on the actual distribution of character states on the phylogeny. For reproductive season, the phylogenetic correlogram shows the relationship between the approximate phylogenetic distance and the correlation for median peak reproductive season. Dashed lines indicate the 95% confidence envelope computed with 1000 bootstraps. Green highlighting on the correlogram shows areas of significance. We reported the trait as having a significant phylogenetic correlation (denoted by an asterisk) if the number of steps fell below the fifth percentile of the distribution (for categorical traits) or $P < 0.05$ (for reproductive season, $P = 0.002$). Image of *Linckia columbiae* by Chris Trent, with permission. All other images available under Creative Commons license CC-BY-3.0, CC-BY-4.0, or CC-BY-SA-4.0.

suggest taxon name replacements for clarity in Table S6 (available online). Although placement of some taxa (as mentioned above) should be interpreted with caution, the phylogeny presented in Figure 1 provides the currently best available framework for this suite of target species on which to explore traits. However, we remind the reader that the purpose of constructing this phylogeny is to explore whether SSW impacts may have a phylogenetic correlation.

Relative SSW impact (Fig. 1)—a proxy for physiological susceptibility to succumb to wasting—does not have a phylogenetic correlation, that is, it is not phylogenetically clustered; the actual number of steps required (11) to explain

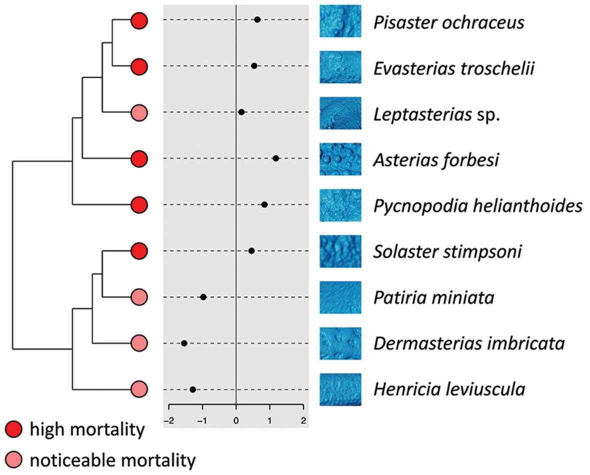

Figure 2. Asteroid rugosity centered, scaled in PhyloSignal, and plotted on an asteroid cladogram (but limited to species for which rugosity was available), with wasting impact indicated by color shading. Rugosity values are from Aquino *et al.* (2021), and images generated using micro-computed tomography were provided by Ian Hewson. Images represent a 0.6-mm segment, with color representing relief. No phylogenetic association was detected in rugosity ($\lambda = 0.788$, $P = 0.119$).

the distribution of SSW character states does not differ substantially from the average number of steps if these states were randomly distributed on the tree (12.5; $n = 999$; Fig. S4, available online). Categorical organization of geographic distribution also lacked a phylogenetic association (Fig. S4). However, developmental mode (actual = 8, $\text{mean}_{\text{random}} = 10.0$) and PLD (actual = 7, $\text{mean}_{\text{random}} = 9.5$) generates interesting results that merit further attention, with trait distributions requiring fewer steps than 0.06 of the randomized distributions (Fig. S4). The categorical traits with the strongest phylogenetic association included diet (actual = 12, $\text{mean}_{\text{random}} = 14.7$) and substrate (actual = 12, $\text{mean}_{\text{random}} = 15.0$); both were in the <4th percentile (Fig. S4). For the continuous traits, phylogenetic association was not indicated with depth (high: $\lambda = 0.028$, $P = 0.814$; low: $\lambda = 0.000$, $P = 1.000$; and median: $\lambda = 0.021$, $P = 0.857$; Fig. S5, available online) or rugosity ($\lambda = 0.788$, $P = 0.119$; Fig. 2). However, phylogenetic association was detected for median month of peak reproductive period ($\lambda = 0.876$, $P = 0.002$) and latitude ($\lambda = 0.715$, $P = 0.046$), although latitude was driven by *Asterias* spp. (Fig. S5). Median peak reproductive month was the only significant ($P < 0.05$) trait after the Benjamini-Hochberg adjustment; however, we report all potentially significant findings regardless of the number of tests because accounting for phylogenetic correlation, particularly in SSW, was a prerequisite for association tests between various traits and SSW in the following section.

Patterns we do (not) find: traits and sea star wasting

After finding no phylogenetic association in SSW impact, we directly compared SSW impact to various traits. Of those traits, we found no clear associations between SSW impact and PLD, developmental mode, diet, substrate, or maximum depth (Table 1). Species reported as having high mortality associated with wasting—that is, *Pisaster ochraceus*, *Pisaster brevispinus*, *Evasterias troschelii*, *Asterias forbesi*, *P. helianthoides*, *Solaster stimpsoni*, and *Solaster dawsoni*—span two different asteroid superorders (Fig. 1); have different diets (Figs. S6, S7, available online), developmental modes, and pelagic durations (Fig. 3); and occupy different substrates and depth profiles (Figs. S6, S7).

Traits that did show an association with SSW impact included minimum depth, median peak reproductive month, and rugosity (Table 1). For the shallow end of the species' depth distributions, species with the shallowest minimum depth were more impacted by SSW relative to species with a deeper minimum depth ($\chi^2 = 10.734$, df = 1, $P = 0.001$; Table 1; Fig. S4, available online). Moreover, species with the highest SSW impact had an earlier median month of reproductive season (about mid-May), whereas species with lower wasting impacts occurred later (about late July) ($t = 2.62$, df = 20, $P = 0.008$; Table 1; Fig. 3A).

Greater rugosity was associated with higher SSW impact ($\chi^2 = 5.406$, df = 1, $P = 0.020$; Table 1; Fig. 2), as indicated in Aquino *et al.* (2021). Although we could explore this relationship in only a subset of taxa ($n = 9$), given limited data availability, we found that rugosity corresponded to wasting impact across two different asteroid orders (Forcipulatida and Valvatida) and that the pattern was not driven by phylogenetic correlation ($\lambda = 0.788$, $P = 0.119$). Species having high mortality associated with wasting—*P. ochraceus*, *E. troschelii*, *A. forbesi*, *P. helianthoides*, and *S. stimpsoni*—all had the highest rugosity values (Fig. 2; also see Oulhen *et al.*, 2022).

Discussion and Rationale

The taxonomic breadth, differential impacts among species, and elusive etiology of SSW have laid bare how little we know about the basic biology and ecology of many sea stars (see Oulhen *et al.*, 2022). Likewise, these challenges have made obvious the opportunities available to advance our understanding of these taxa and of marine mass mortalities and wildlife diseases more generally. Critical to this effort is understanding the broader evolutionary context in which these ecological dynamics are playing out. As a synthetic exploration of what can be determined from available data, our work suggests some organismal trait associations that may aid further monitoring or experimental programs in studying SSW in regions that have been less intensely studied and identifies gaps in knowledge that should be filled.

Sea star wasting across species in the context of asteroid traits

Results generated here provide a framework that compiles available natural and life-history data with SSW occurrence, while testing for a phylogenetic association. Sea star wasting varies in severity across the tree and lacks clear

Table 1

List of traits for which we tested for phylogenetic associations and then those tested for an association with sea star wasting (SSW) impact

Trait	Phylogenetic association test[a]	SSW-trait association test	Description of SSW-trait comparison	Result
Categorical				
SSW	11, 12.5 (0.167)	—		
repro_season	4, 4.8 (0.162)	—		
PLD	7, 9.5 (0.052)	χ^2 = 0.265, df = 2 (0.867)	dev_mode: none (0 days), shorter (>65), longer (≥85); SSW: low, high	No relationship
dev_mode	8, 10.0 (0.057)	χ^2 = 8.259, df = 15 (0.913)	See footnote b	No relationship
diet	**12, 14.7 (0.029)**	χ^2 = 12.719, df = 23 (0.958)	See footnote b	No relationship
substrate	**12, 15.0 (0.035)**	χ^2 = 6.612, df = 15 (0.968)	See footnote b	No relationship
lat_5groups	14, 14.7 (0.404)	—		
lat_9groups	18, 19.3 (0.212)	—		
Continuous				
depth_median	0.021 (0.857)	—		
depth_max	0.028 (0.814)	χ^2 = 0.952, df = 1 (0.329)	depth_max: shallow (≤100m), deep (≥250m); SSW: low, high	No relationship
depth_min	0.000 (1.000)	**χ^2 = 10.734, df = 1 (0.001)***	depth_min: shallow (≤0.5m), deep (≥5m); SSW: low, high	Higher SSW impact in shallow *vs.* deeper species
rugosity	0.788 (0.119)	**χ^2 = 5.406, df = 1 (0.020)**	rugosity: low (≤0.40), high (≥0.42); SSW: low, high	Higher SSW impact in more *vs.* less rugose species
repro_season	**0.876 (0.002)***	***t* = 2.62, df = 20 (0.008)***	SSW: low, high; repro_season: test for different median peak month	Higher SSW impact in spring spawners than later spawners
lat_dim1	**0.715 (0.046)**	—		

For traits handled as categorical—SSW impact, reproductive season, pelagic larval duration (PLD), developmental mode, diet, substrate, and latitude (broken into either five or nine groups)—we tested for phylogenetic association by comparing the actual number of steps required to explain the distribution of character states to the average number of steps required if character states were randomly distributed across the tree (calculated for 999 runs). For continuous traits—depth (minimum, maximum, and median), rugosity, and reproductive season (*i.e.*, peak reproductive month)—we tested for phylogenetic associations by using Pagel's λ. Significant values are bolded (*i.e.*, falling below the fifth percentile for categorical traits and $P < 0.05$ for continuous traits). After determining there was no significant phylogenetic association in SSW, we tested for associations between SSW impact and various traits, using either a chi-squared or a *t* test as summarized in the table. The results of the association tests are listed in the final column.

[a] For categorical traits, the first number listed is the actual number of steps required to produce the distribution of character states on the tree, the second number is the mean number of steps required to produce a random distribution of character states, and parenthetically is the proportion of runs (of 999) that fall below the actual value. For continuous traits, Pagel's λ is shown with the *P*-value in parentheses.

[b] For these traits we had no a *priori* expectation about a specific relationship with SSW, so we compared the distribution of possible character state pairs between SSW and each trait with the actual distribution of character state pairs and used a chi-squared test to test whether they were different.

* Significant after Benjamini-Hochberg adjustment.

phylogenetic correlation at this level, while other traits vary in their degree of phylogenetic correlation and relationship to SSW. These divergent patterns provide clues about physical and environmental associations of specific traits that may guide advances in SSW research.

Our analyses highlight two facets of SSW that merit further exploration. First, the impact of this disease spans asteroid diversity (Fig. 1; Fig. S1, available online) and shows no clear association to a particular substrate, diet, or developmental mode (Table 1; Fig. 3; Figs. S6, S7, available online). This suggests that there may be specific elements of being a sea star that have made them susceptible to new features appearing in their environment, whether pathogenic or not. All asteroids, as echinoderms, represent the largest clade that is neither terrestrial nor in freshwater, which indicates that they are sensitive to a certain range of environmental parameters (see Oulhen *et al.*, 2022). The sensitivity of these organisms to their environment despite their ubiquity in marine ecosystems is intriguing because it may presage susceptibility to certain environmental extremes, which also varies across species (Hemery *et al.*, 2016).

Second, three traits showed a potential relationship with SSW: minimum depth, reproductive season, and rugosity. Although maximum depth showed no relationship to SSW (Table 1), species with the shallowest minimum depth (*e.g.*, higher in the intertidal distribution) tended to have greater SSW impacts relative to species with deeper minimum depths (Table 1; Fig. S4, available online). This finding is consistent with historical accounts of wasting that documented higher mortality at shallower depths (Dungan *et al.*, 1982) and with implications from new taxonomically broad analyses of the mid-2010s SSW outbreak (M. N Dawson *et al.*, unpubl. data). A novel finding of our study is the apparent difference in the average median reproductive month between species with higher SSW impacts (mid-May) *versus* lower SSW impacts (late July) (Table 1; Fig. 2A). In the Salish Sea (Washington), peak wasting prevalence occurred in August 2014 (after building over the summer) in *Pycnopodia helianthoides*, *Evasterias troschelii*, and *Henricia* spp., all species

Figure 3. Asteroid life-history traits hypothesized to have a relationship with sea star wasting (SSW) plotted with SSW impact by species. (A) Reproductive season for various asteroid species. Letters in the inner circle represent months, and shading represents seasons. Gray bars indicate reproductive season, and black bars indicate peak reproductive season. Each species is labeled at the approximate midpoint for its documented reproductive season, with the label color indicating species with "noticeable" and "high mortality." Developmental mode plotted with corresponding SSW impact (B) and pelagic larval duration (PLD; C).

classified in this paper as being significantly affected by SSW (*i.e.*, noticeable or high mortality) and having earlier reproductive periods. Likewise, in *Pisaster ochraceus*—which had high SSW-associated mortality and has an early reproductive season (Fig. 3A)—Menge *et al.* (2016) found that high SSW prevalence persisted into the late fall in 2014 before declining over winter, re-emerging in spring and summer and building again to outbreak levels in late summer at a subset of sites in Oregon. The seasonal component of SSW outbreaks and the increased wasting impact seen in species with earlier seasonal reproduction, combined with previous observations that smaller (*i.e.*, non-reproductive individuals) are less likely to develop and die from wasting (though detection may be harder in small stars) (Menge *et al.*, 2016), warrant further investigation. Timing of resource allocation shifts to or away from gonad development may play a potential role in promoting vulnerability to SSW, but this remains to be explored. Although the relationships between SSW and reproductive season and depth are suggestive, it is important to note that shallower species tend to span the full range of seasonal reproductive periods, whereas deeper-water taxa tend to have reproductive periods later in the year (Fig. 3A; Table S3, available online); and so additional work is encouraged to disentangle the influence of depth *versus* reproductive season. Moreover, temperature is an additional axis of variation; and although outside the scope of this paper, temperature differences are inherent across depth gradients and seasons and warrant further investigation.

Intriguingly, the third trait—dermal rugosity—which seems to not be phylogenetically correlated (Fig. 2) but which is based on limited available data, appears to be predictive of the severity of effects of SSW on a species (Aquino *et al.*, 2021). Although data limitations restricted our analysis to a small sample of asteroid diversity, the lack of phylogenetic association implicates an environmental factor, not inconsistent with the hypothesis that dermal rugosity promotes dysoxia-driven microbial dysbiosis—whether pathogenic or not—on sub-millimeter scales at the epidermis that leads to hypoxia and wasting (Aquino *et al.*, 2021). The impacts of greater rugosity may be twofold: (1) altering gas exchange across the animal-sea interface, leading to an imbalance of what is needed for effective respiration; or (2) providing depressed refuges that protect infections or opportunistic pathogens from hydrodynamic turbulence (Crawford *et al.*, 2012; Achinas *et al.*, 2019). Both mechanisms could leave species with greater rugosity more vulnerable to SSW in certain environmental conditions—such as increased productivity during enhanced upwelling (Aquino *et al.*, 2021; but see M. N Dawson *et al.*, unpubl. data)—even in (or particularly in) intertidal communities, where oxygen is not thought to be limiting at the macroscale. Evidence of higher SSW mortality at less energetic sites is consistent with local-scale abiotic environmental modulation of wasting risk (see M. N Dawson *et al.*, unpubl. data).

Mass mortalities in a broader context

Despite a tremendous flurry of post-SSW research into basic components of echinoderm biology, physiology, demography, growth, and genomic response to the environment (Ruiz-Ramos *et al.*, 2020; Oulhen *et al.*, 2022), more needs to be known; and consideration of sea star phylogeny is needed, given the taxonomic breadth of SSW-affected species. Our work suggests that some organismal traits may provide new insights into differential impacts on these species. We still do not know the etiology of this major wildlife epizootic pandemic that has serious ecological ramifications (Menge *et al.*, 2016; Schultz *et al.*, 2016; Gravem and Morgan, 2017; Eisaguirre *et al.*, 2020). That certain aspects of biology may predispose sea stars to abiotically influenced disease in a subset of environments is useful but incomplete information and needs a broader context. While individual species that occur in intertidal habitats are, almost by definition, sufficiently adapted to conditions of the intertidal, the effects of SSW appear most severe at this terrestrial-marine interface that is marginal for the clade (*i.e.*, variously marine, terrestrial, and freshwater when it rains) and that is experiencing more environmental variability with accelerating global change. As an example, it beckons the question whether intertidal populations of other species elsewhere—without funded monitoring programs like the west coast of North America—are also prone to wasting. Additionally, species with different propensities to waste under similar (intertidal) conditions could be assessed for variation in activity of particular cellular pathways. Only with relevant phylogenetically and ecologically correct estimates—which may come in a variety of forms (Felsenstein, 1985; Dawson, 2014)—can we specifically assess phenotypic traits that may provide the insight necessary to learn the causes of SSW mass mortality events, so more inclusive phylogenies are needed.

Importantly, the phylogenetic breadth of species suffering from SSW and the ubiquity of risk factors, such as being intertidal, encourages us to consider the potential implications. For example, chytrid fungal infections span all known anurans, have led to mass die-offs and extinctions, and are exacerbated by environmental fluctuations (Raffel *et al.*, 2013). Phylogenetic analyses helped detect the geographic origin of the disease and discover that, where the infection originated, species had co-evolved with the fungus and even developed resistance (Fu and Waldman, 2019; Fisher and Garner, 2020). Understanding which species are resistant, and why, can reciprocally point toward which species may have greater disease risk and their risk factors, which can help inform conservation priorities.

Signatures of wildlife disease breadth and prevalence are typically elusive unless clear human consequences catalyze research to fill knowledge gaps. For example, although the mass die-off of the sea urchin *Diadema antillarum* in the 1980s (Lessios, Robertson, and Cubit, 1984) transformed the biodiversity and ecology of the Caribbean, the cause remains entirely unknown (Carpenter, 1990; Edmunds and Carpenter, 2001). In contrast, the dramatic loss of the economically impactful American chestnut in the early twentieth century has a well-documented history including early spatial, population-level origins, which led to a detailed etiology as well as a potential recovery plan. Though the two examples are replete with differences—the human relevance, the kingdom, the realm, and so on—the key difference is perhaps microevolutionary rather than macroevolutionary. To fully understand SSW and its origins, we will likely need to know more about the earliest responses and susceptibilities among individuals within species to understand how variation modulates SSW and whether this is similar across species.

Future directions in studying asteroid mass mortality events

Although we provide a first step toward building a more complete picture of the relationships between SSW and life-history and natural history traits, an equally important outcome of our study has been to reveal how incomplete our basic knowledge is. This review takes the stage as whole-genome sequencing and deep evaluation of population genomic dynamics, even in non-model systems, has become feasible and more common (Ellegren, 2014; Choquet *et al.*, 2019). Such resources have huge potential to facilitate conservation efforts (Shaffer *et al.*, 2022). In addition to resolving phylogenetic relationships of Asteroidea by using transcriptome-level data (*e.g.*, Linchangco *et al.*, 2017), whole genome-scale data are becoming more widely available in Asteroidea, permitting strategic contrasts between intra- and interspecific genomic diversity that pave the way for understanding the genomic factors underpinning SSW vulnerability. Are there parallel patterns of selection and differential gene expression between different species impacted by SSW, implicating shared genomic regions influencing vulnerability to SSW? Moreover, epigenetic mechanisms (non-heritable genomic modifiers influencing gene expression and regulation) can contribute to genetic assimilation, where selection can drive a trait to become less plastic through genetic fixation (Schneider and Meyer, 2017).

Targeting specific groups or pairs of species that are closely related but that differ in life history or environment will be invaluable for clarifying the roles of life history and environment in wasting—for example, *Henricia* spp. (different reproductive strategies and tidal heights), *Pycnopodia helianthoides* and *Rathbunaster californicus* (sister taxa, but different, mostly non-overlapping, depth ranges), *Pisaster* spp. (largely co-distributed, but different wasting impacts, depths, and, to some, degree diet), and *Leptasterias* spp. (where one could explore impacts of SSW on multiple geographically overlapping lineages). Comparative genomic analysis of strategic contrasts could reveal genetic pathways activated during wasting and whether those pathways differ between species or are shared. If particular advantageous alleles and traits are associated with greater survivorship, these should, through time, increase in frequency under wasting pressure. In addition, epigenomics represents an underexplored area of research and has been shown to play a critical role during times of environmental stress (Feil and Fraga, 2012; Fabrizio *et al.*, 2019; Byrne *et al.*, 2020). However, genomic and epigenomic tools must be coupled carefully with studies of biology, ecology, and environment. We need to build a comprehensive picture of how genetic and other heritable and non-heritable diversity interact in the context of MMEs over time through coupled eco-genetic monitoring of populations. This pursuit will fill key knowledge gaps and help narrow the likely cause(s) of SSW while also yielding similar benefits for the study of future, as yet unappreciated, threats during this time of rapid global change.

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