Science of the Total Environment 449 (2013) 150–156

Contents lists available at SciVerse ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

A meta-analysis of the effects of pesticides and fertilizers on survival and growth of amphibians

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HIGHLIGHTS

- ► We used meta-analytic techniques to examine agro-chemical impacts on amphibians.
- ► We looked at survival and growth metrics for available amphibian data.
- ► Pesticides and fertilizers negatively impacted amphibian survival.
- ► Pesticides and fertilizers negatively impacted amphibian growth.

ARTICLE INFO

Article history:
Received 22 June 2012
Received in revised form 16 January 2013
Accepted 18 January 2013
Available online 16 February 2013

Keywords:
Meta-analysis
Pesticide
Fertilizer
Amphibian
Agrochemical

ABSTRACT

The input of agrochemicals has contributed to alteration of community composition in managed and associated natural systems, including amphibian biodiversity. Pesticides and fertilizers negatively affect many amphibian species and can cause mortality and sublethal effects, such as reduced growth and increased susceptibility to disease. However, the effect of pesticides and fertilizers varies among amphibian species. We used meta-analytic techniques to quantify the lethal and sublethal effects of pesticides and fertilizers on amphibians in an effort to review the published work to date and produce generalized conclusions. We found that pesticides and fertilizers had a negative effect on survival of −0.9027 and growth of −0.0737 across all reported amphibian species. We also observed differences between chemical classes in their impact on amphibians: inorganic fertilizers, organophosphates, chloropyridinyl, phosphonoglycines, carbamates, and triazines negatively affected amphibian survival, while organophosphates and phosphonoglycines negatively affected amphibian growth. Our results suggest that pesticides and fertilizers are an important stressor for amphibians in agriculturally dominated systems. Furthermore, certain chemical classes are more likely to harm amphibians. Best management practices in agroecosystems should incorporate amphibian species-specific response to agrochemicals as well as life stage dependent susceptibility to best conserve amphibian biodiversity in these landscapes.

1. Introduction

Anthropogenic impacts on natural systems are of growing concern as human populations expand and global biological diversity declines (Benton, 2007; Donald and Evans, 2006). Among the many stressors attributed to humans, chemical contaminants are anthropogenically created, used, and distributed, and may pose significant risk to a variety of taxa and ecosystems (Relyea, 2005b). Agricultural practices often occur near freshwater ecosystems, which put these freshwater systems at a high risk for chemical exposure. Direct and indirect pathways exist for exposure of freshwater systems, such as intentional application for pest control, accidental overspray, runoff, leaching, and sediment deposition (Boone et al., 2005; Relyea, 2005a, 2005b, 2005c).

Several groups of non-target organisms have been found to be highly sensitive to pesticide exposure, including amphibians, crustaceans, bivalves, nematodes, annelid worms, and non-target insects (Kerby et al., 2010). Although amphibian and fish species tend to be less susceptible to pesticide and fertilizer exposure than invertebrate species, there is evidence of significant negative effects on survival and growth (Davidson et al., 2002; Kerby et al., 2010; Relyea, 2005a; Shelley et al., 2009). Impacts on amphibians are of particular interest because amphibian population declines are occurring worldwide (Alford and Richards, 1999; Blaustein et al., 1994; Mendelson et al., 2006; Stuart et al., 2004). Additionally, many amphibian species are data deficient, meaning we cannot accurately assess their conservation status (Stuart

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0048-9697/$ – see front matter
http://dx.doi.org/10.1016/j.scitotenv.2013.01.056

et al., 2004). Investigating stressors such as pesticides and fertilizers may help fill in knowledge gaps and potentially contribute to amphibian conservation efforts worldwide.

The effects of pesticides and fertilizers on amphibians include increased mortality, reduced growth, developmental abnormalities, and increased susceptibility to disease (e.g., Boone and Bridges, 2003; Mills, 2004; Relyea, 2005a). The effect of these chemicals can vary among chemical classes and species. For example, survival of the green frog (*Rana clamitans*) decreased when exposed to Abate®, an organophosphate pesticide, whereas Release, a chloropyridinyl pesticide, did not result in decreased survival in the same species (Sparling et al., 1997; Wojtaszek et al., 2005). In addition, carbaryl, a carbamate pesticide, negatively impacted survival of the spotted salamander (*Ambystoma maculatum*) but did not impact the survival of the southern leopard frog (*Rana sphenocephala*) (Boone and James, 2003; Boone et al., 2004).

Sublethal impacts can include longer larval periods, smaller size at metamorphosis, and increased susceptibility to predation due to decreased swim speed and endurance (Boone and Bridges, 2006; Mills, 2004). Additionally, indirect impacts on growth can be attributed to food web disruptions initiated by these chemicals. Herbicides may also decrease primary production, resulting in increased competition and reduced growth rates (Boone and Bridges, 2003; Relyea, 2006; Relyea and Diecks, 2008).

We posit that a comprehensive look at the effects of pesticides and fertilizers on amphibians would better direct management and conservation decisions worldwide. Most studies focus on single chemicals or species, and quantify only the LC50 (lowest concentration needed to kill 50% of the test subjects; Relyea, 2004). With hundreds of pesticides and dozens of fertilizers in use (Gail and Leonard, 2000), a comprehensive approach is needed to quantify effects of these chemicals on amphibians.

Here, we used a meta-analytic technique to synthesize published studies on lethal and sublethal impacts of pesticides and fertilizers on amphibian species worldwide. Meta-analytic techniques are the most statistically rigorous method for summarizing independent data (Bancroft et al., 2008; Gurevitch et al., 1992) and hence are ideal for reviewing lethal and sublethal impacts of chemical contaminants on amphibians. We quantified the overall effect of 16 classes of chemicals, representing both pesticides and fertilizers, on survival and growth of amphibians. Chemicals were analyzed as groups based on parent chemical classes. Chemical classes were defined as groups of chemicals that have similar structures and activity (Kegley et al., 2008) and this allowed for a more generalized representation of the chemicals used in previous studies (Table 1). We hypothesized that pesticides and fertilizers would have an overall negative effect on growth and survival in amphibians and that chemical classes would differ in their effects on both survival and growth.

2. Methods

2.1. Data selection

We used five databases to identify studies for analysis (Aquatic Sciences and Fisheries Abstract, BIOSIS, Environmental Sciences and Pollution Management, Web of Science, and Wildlife and Ecology Studies Worldwide). To find primary literature on the effects of agricultural chemicals on amphibians within these databases, we searched for all combinations of five search terms: pesticide or fertilizer, survival, growth, mortality, and amphibian. We limited our search to experimental manipulations of pesticides and fertilizers. To avoid potential biases in the selection of studies, we established a priori criteria for the inclusion of studies in the meta-analysis: 1) each study must give the mean survival or growth data for both an experimental group (chemical exposed) and an appropriate control group (no chemical exposure), 2) each study must give the sample size for both the experimental group and control group, and 3) chemical concentrations must be ecologically relevant, which means that they must be within a range of possible concentrations that one would expect to see in the environment after a spray event (Table 1). Any data points within an article that met these criteria were considered for inclusion.

Table 1
Summary of pesticides and fertilizers used in the meta-analysis organized by chemical classes, chemicals, and expected environmental concentrations (EEC) represented as mg/L.

Chemical class	Chemical	EEC	References
Carbamate	Carbaryl	5	Boone and Bridges (2003)
Chloro-nicotinyl	Imidaclorpid	42	EPA (1992)
Chlorophenoxy acid	2,4-D	0.12	Relyea (2005c)
Chloropyridinyl	Release	5.77	Wojtaszek et al. (2005)
Dithiocarbamate	Mancozeb	0.008	Harris et al. (2000)
Inorganic fertilizers	Calcium	15	Hammer et al. (2004)
	Phosphate	50	WHO (2007)
	Nitrate	50	WHO (2007)
Organochloride	Endosulfan	10	Harris et al. (2000)
Organophosphorus	Malathion	1.8	Relyea and Diecks (2008)
	Abate	0.05	EPA (1998)
	Chlorpyrifos	0.0037	Wood and Stark (2002)
	Diazinon	0.082	EPA (2005)
Organotin	Triphenyltin	0.002	Fioramonti et al. (1997)
Phenol	Octylphenol	0.05	Rohr et al. (2003)
Polyalkyloxy compound	POEA	0.6	Howe et al. (2004)
Pyrethroid	Permethrin	0.05	Johansson et al. (2006)
	Alpha-cypermethrin	0.006	Greulich and Pflugmacher (2003)
Triazine	Atrazine	0.002	Boone and Bridges (2006)
	Cyanazine	0.9	Johansson et al. (2006)
Urea	Urea	154	Schuytema and Nebeker (1999)
	Diuron	10	Schuytema and Nebeker (1998)
Other	Methoprene	0.05	Chu et al. (1997)
	Azadiracthin	0.5	Punzo (1997)

Several studies included more than one species, chemical, dose, or sampling period. All species and chemicals from a given study were included in our analyses if the overall inclusion criteria were met. Although including all species or chemicals from one study might decrease the independence among some data points, the inclusion of all available species and chemicals allowed us to more fully explore the effects of pesticides and fertilizers in these systems (Bancroft et al., 2007). However, if more than one dose of the same chemical was used in the original article, we then randomly selected only one dose level for inclusion in our analysis. If the study reported survival or growth over a time series, we selected the final measurement for analysis. When studies quantified growth using several response variables (i.e., length and mass), we randomly selected one variable for inclusion. All data were obtained from primary research articles and, when necessary, data were extracted from published figures using TechDig V.2.0 software.

2.2. Effect sizes

To calculate an overall measure of pesticide and fertilizer effect on survival and growth in amphibians, including magnitude and direction (positive or negative), we used a log response ratio (lnR) as our metric of standardized effect size (Hedges et al., 1999). We defined the control group as the group not exposed to any pesticides or fertilizers; therefore, a negative value in our response ratio indicates a negative effect of pesticides and fertilizers on survival or growth. MetaWin Version 2.0 (Rosenberg et al., 2000) was used to generate effect sizes and confidence intervals. Because some studies did not include a measure of error, and we wanted to include as many studies as possible, we weighted effect sizes by sample size following methods outlined in Wu et al. (2011). Normality assumptions were checked via normal Q–Q plots. MetaWin Version 2.0 was used for all analyses.

2.3. Full models

Response variables were selected with the intention of quantifying both lethal and sublethal effects. To accomplish this, we ran two separate analyses quantifying survival and growth effects. Survival was selected as a response variable because the majority of studies have quantified amphibian mortality at various levels of pesticide and fertilizer exposure. Growth was chosen because it is used to quantify sublethal effects and is often measured in conjunction with survival.

Fixed effects and random effects models were then used to calculate the grand mean effect size for each analysis. Some authors suggest using fixed effects models initially, and then using a random effects model if significant heterogeneity is observed in the fixed effects model (Hedges and Vevea, 1998). Our results will report both the fixed and random effects models, however, we will focus on the random effects models because we believed that the studies collected were not conducted in the same manner and that these studies may differ in ways that would have impacted the results, and therefore we should not assume a common effect size as we would in a fixed effects model. Using a random effects model also allows us to draw conclusions more broadly as we can view the studies collected as a subset of the population (Borenstein et al., 2009). The output of each statistical test consisted of the grand mean effect size for the analysis with an accompanying biased-corrected bootstrapped 95% confidence interval (CI) (Adams et al., 1997). Because of the distribution of our effect sizes biased–corrected bootstrapped 95% confidence intervals are the most conservative estimate of error. The mean effect is significantly different from zero if the CIs do not overlap with zero.

2.4. Chemical class analysis

In addition to examining effect size on survival and growth, we were interested in examining how effect sizes varied amongst different classes of chemicals. Chemical classes represent groups of chemicals that share similar structure and behave both environmentally and physiologically in similar ways (Kegley et al., 2008). The mode of action of each chemical varies by the type of chemical class. For example, carbamates and organophosphates are cholinesterase inhibitors, pyrethrins are ion channel manipulators, and organochlorines are endocrine and chloride channel disrupters (Kegley et al., 2008). We compared the mean effect size between chemical classes, using a mixed-effects model, in both survival and growth studies. A mean effect size, bias-corrected bootstrapped 95% CI, and standard error were calculated for each group in the chemical class analyses and groups with fewer than four comparisons were removed. Survival and growth studies were analyzed separately.

2.5. Publication bias

The potential effect of publication bias, commonly referred to as the File Drawer Problem (Rosenthal, 1979), was tested using Rosenthal's failsafe number (Rosenthal, 1979). The failsafe number is a quantitative representation of the importance of publication bias to the outcome of our analyses. Rosenthal's failsafe number is the number of missing studies with a mean zero effect size necessary to change the results of an analysis from significant to non-significant. A robust failsafe number is considered anything above $(5*n+10)$ where n equals the number of studies (Rosenberg, 2005). Total number of studies in the survival and growth analyses was 66 and 45 respectively. Rosenthal's failsafe number was large for survival (1712.7) and was zero (0.0) for growth, which indicates that publication bias is not likely to influence the outcome of the survival analysis but could influence the outcome of the growth analysis. If publication is biased towards publishing only those manuscripts with significant effects on growth, our results may over-estimate the effects of pesticides and fertilizers on growth. In addition to the failsafe number, funnel plots of the effect sizes were generated for both survival and growth. The distribution of the effect sizes in the funnel plots did not show significant asymmetry, which supports our assertion that publication bias is not likely to influence our results for the survival analysis and suggests that publication bias may be only a minor problem for the growth analysis.

3. Results

We collected and synthesized the results from 66 survival studies (186 comparisons) and 45 (97 comparisons) growth studies and found an overall negative effect of the chemicals examined on both the survival and growth of amphibians. We found that exposure to pesticides and nitrogen-based fertilizers resulted in an effect size of −0.9027 (95% CI: −1.2555 to −0.5623), which represents a significant negative effect on survival compared with controls (Fig. 1). For growth, we found that exposure to pesticides and nitrogen-based fertilizers resulted in an effect size of −0.0737 (95% CI: −0.1614 to −0.0041), which represents a significant negative effect on growth compared with controls (Fig. 1).

There was significant heterogeneity in the fixed effects model for survival, ($Q=506.86$, p-value<0.001, $df=185$). This result indicates that there is more variation in the studies than due to sampling error alone, which suggests that a random effects model should be used to explore moderators of this variation among chemical classes. The fixed effects model for growth, however, did not show any significant heterogeneity ($Q=12.21$, p-value$=1.00$, $df=96$), which indicates that the variation in the studies is what we would expect due to sampling error alone. We suggest, however, that because these studies came from a variety of locations, almost certainly using distinct protocols, that we cannot assume that each study was conducted in the exact same way. Furthermore, as above, we wished to draw conclusions beyond the studies in the analysis. Thus, even with heterogeneity statistics that are non-significant for growth, we used a random effects model for this analysis. Results for the fixed effects model for survival and growth can be found in Appendix A.

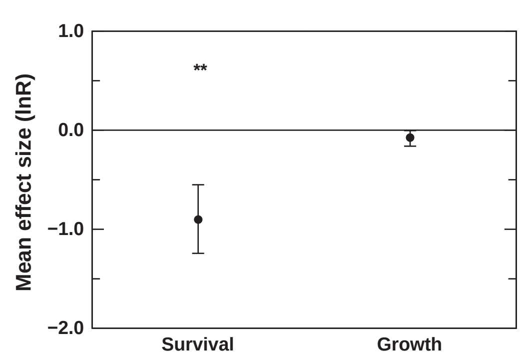

Fig. 1. Grand mean effect size (log response ratio) and 95% confidence intervals of the effect of pesticides and fertilizers on amphibian survival and growth. Solid line represents zero effect. Survival and growth are both significantly lower when amphibians are exposed to pesticides and fertilizers, significant effect sizes denoted by an asterisk. Confidence intervals are bias-corrected and bootstrapped.

There was significant between-group heterogeneity present in the random effects model for the survival analysis (between-group Q = 51.7880, p-value < 0.001, df = 10) but not in the growth analysis (between-group Q = 14.5641, p-value = 0.0682, df = 8) suggesting that there are underlying groups driving differences in effect size for the survival analysis but not the growth analysis. However, we had decided a priori to explore the effect of chemical class on both survival and growth so the growth effects will be reported.

Our results from the chemical class analysis indicate that there were six chemical classes with significant negative effects on survival. Exposure to chemicals in the phosphonoglycine class (with POEA surfactant) resulted in an effect size of −4.3253 (95% CI: −6.0842 to −2.6693), while exposure to carbamate, chloropyridinyl, inorganic chemicals, organophosphate, and triazine, resulted in an effect size of −0.3289 (95% CI: −0.8601 to −0.0506), −0.1279 (95% CI: −0.3567 to −0.0023), −0.6591 (95% CI: −1.2253 to −0.2509), −0.3105 (95% CI: −0.8719 to −0.0648), and −0.9182 (95% CI: −3.1143 to −0.0232) respectively (Fig. 2). Significant differences among chemical classes were observed (Q = 77.958 p-value = < 0.001 between groups, and within group: Q = 175.985 p-value = 0.529.)

Our results from the chemical class analysis on growth showed that there were two chemical classes that have a significant negative effect on growth. Organophosphates had a negative effect size on growth of −0.3419 (95% CI: −0.6954 to −0.1707), while phosphonoglycine (with POEA surfactant) had a negative effect size of −0.1032 (95% CI: −0.2433 to −0.0089) on growth (Fig. 3). No significant differences were observed among groups (Q = 1.1967, p-value = 0.97705 for between groups, and within group statistics: Q = 11.008, p-value = 1.00).

3.1. Sensitivity analysis

We conducted a sensitivity analysis to test whether extreme values were significantly impacting the results of our study. We removed all observations that were more than two standard deviations from the mean and ran the analyses again. The results for both survival and growth were qualitatively the same without these studies included in the analysis, suggesting that a few extreme studies are not driving the results we observed.

Over one-third (34%) of the comparisons in the survival analysis and 23% of the comparisons in the growth analysis were from the work of Rick Relyea and colleagues. To explore the possibility of bias, we removed all comparisons generated by these researchers and ran the analyses again. Our model for survival was qualitatively the same without studies conducted by this group. Without the Relyea laboratory comparisons in the analysis, pesticides and fertilizers still had an over-all negative effect of −0.5955 on survival (95% CI: −1.0179 to −0.3034), compared to −0.9027 (95% CI: −1.2555 to −0.5623) with all studies included in the analysis. However, removing the Relyea-generated data from the growth analysis produced results that differed from the full data set. Without the Relyea-generated data, the effect on growth was −0.0104 (95% CI: −0.1090 to 0.0674), compared to −0.0737 (95% CI: −0.1614 to −0.0041), with all studies included in the analysis. For the growth analysis, because the confidence intervals cross zero, there was no significant effect of pesticides and fertilizers on growth without the Relyea-generated data. However, the exclusion of the Relyea laboratory data removed 30% of the observations from the carbamate chemical class, 50% of the observations from the organophosphate chemical class, and 86% of the observations from the phosphonoglycine class. The removal of more than 50% of the data points from two chemical classes reduces the overall power to estimate the effect of these chemicals on amphibian growth. While it is clear that the Relyea-generated data are influencing the original analysis, the loss of these data points equates to a substantial loss of the total data available, thus an analysis run without those observations is not comparable to the full data set.

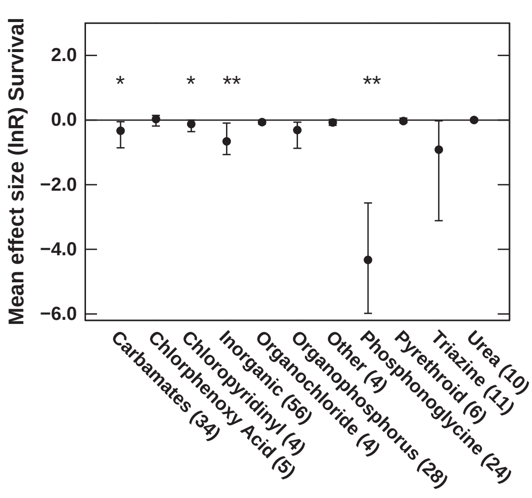

Fig. 2. Mean effect size (log response ratio) and 95% confidence intervals of the effect of chemical classes on amphibian survival. Solid line represents zero effect. The number of comparisons is indicated by the value in the parentheses. Significant effect sizes are denoted by an asterisk. Confidence intervals are bias-corrected and bootstrapped.

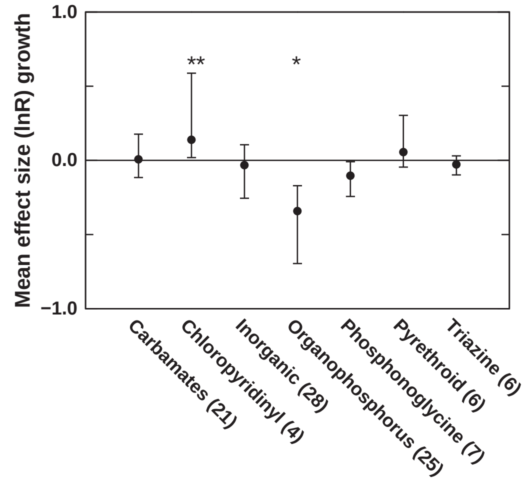

Fig. 3. Mean effect size (log response ratio) and 95% confidence intervals of the effect of chemical classes on amphibian growth. Solid line represents zero effect. The number of comparisons is indicated by the value in the parentheses. Significant effect sizes are denoted by an asterisk. Confidence intervals are bias-corrected and bootstrapped.

4. Discussion

Our synthesis found that exposure to pesticides and fertilizers resulted in a negative effect size of −0.9027 on survival and a negative effect size of −0.0737 on growth of amphibians across all chemicals. When breaking down these findings by chemical class, six classes of chemicals (carbamates, chloropyridinyls, inorganic fertilizers, organophosphates, phosphonoglycines, and triazines) significantly reduced amphibian survival. It should be noted, however, that the studies included in the phosphonoglycine chemical class used chemicals that included the polyoxyethyleneamine (POEA) surfactant, which has been shown to increase the toxicity of these chemicals in non-target species (Relyea, 2005b). The studies using pesticides and fertilizers from these chemical classes represent approximately 55% of the total survival observations in this analysis. Two chemical classes (organophosphates and phosphonoglycine) reduced amphibian growth, representing 31% of the total growth observations.

Organophosphates, triazines, and phosphonoglycines rank amongst the most prevalent chemical classes used in the United States and can reach a combined total of over 180 million pounds of active ingredient used each year (Gail and Leonard, 2000). In addition, more than 45 billion tons of inorganic fertilizers are used each year, and this number was predicted to increase (Lanyon, 1996; USDA, 2006). Compounding their prevalence, these chemicals often are applied multiple times during the spring agricultural growing season; amphibians typically breed in the spring, thereby increasing the chance of exposure during the sensitive larval and embryonic life stages (Cox et al., 2006; Ortiz and Sparling, 2007; Relyea and Diecks, 2008). Precision application techniques can be used to limit overspray and leeching of chemicals into aquatic habitats that abut or are near to agricultural fields, and timing agrochemical application should ideally align with non-breeding seasons for endemic amphibian species.

Our results indicate that the application of some pesticide chemical classes can lead to a decrease in amphibian survival and growth which in turn can have negative consequences on biological communities in many different biomes. A significant reduction in amphibian survival may eventually lead to population and community level changes via alterations in foraging rates (Walls and Williams, 2001; Whiles et al., 2006) and available biomass for potential predators (Rodenhouse et al., 2009). Negative impacts of chemical contaminants on amphibian growth rates may result in delayed metamorphosis and/or smaller size at metamorphosis. Any delay in metamorphosis has the potential to increase susceptibility to predation, negatively impact on reproductive success, and result in failure to emerge from an ephemeral water body (Berrill et al., 1993). Unfortunately, predicting specific impacts of pesticide and fertilizer exposure on amphibian assemblages is difficult because survival rates are often species-specific (Boone and Semlitsch, 2001). As such, there is potential for selection for resistant species at sites regularly exposed to pesticides and fertilizers species, which could alter community composition over time (Boone and Semlitsch, 2002).

Best management practices for chemical application in agricultural ecosystems can have profound impacts on amphibian survival and growth. Amphibians have stage dependent responses to many pesticides, thus it is important to consider developmental stage when designing pesticide and fertilizer application protocols and testing for contaminant sensitivity (Harris et al., 2000). Most studies looking at amphibian sensitivity to pesticides and fertilizers focus on the larval stage; this is evident in our analysis as approximately 93% of the studies quantified larval response variables. More work is needed on the embryonic and post-metamorphic life stages before a comprehensive analysis on these life history stages can be completed (Relyea, 2005c). Small modifications in agricultural practices, like using alternative chemicals, spraying at different times, and even using less of these chemicals are all options that could be implemented to help improve native communities.

While many of the studies used in our analysis test for direct effects of pesticides and fertilizers on amphibian growth and survival, published studies quantifying indirect effects are sorely lacking (a notable exception is Rohr and McCoy, 2010). Furthermore, interactions between contaminants and other environmental factors have been shown to negatively impact amphibians and more realistically depict complex habitat conditions (Bancroft et al., 2008). For example, several studies suggest that the presence of predator cues can interact synergistically with pesticides (Boone and Bridges, 2006; Relyea, 2005b, 2005c; Relyea and Mills, 2001). Nitrates have been shown to act synergistically with ultraviolet-B radiation to lower growth in *Pseudacris regilla* (Hatch and Blaustein, 2003). Pesticides may also increase the risk of parasitic infection. In a study conducted by Kiesecker (2002), amphibians exposed to agricultural runoff had a higher proportion of parasitic cysts relative to controls.

In addition to interactions with natural stressors, synergistic effects of multiple pesticides and fertilizers can occur if applied in combination (Hayes et al., 2006). Few laboratory studies and even fewer field studies look at the combined effects of exposure to multiple pesticides. In addition, it is poorly understood how chronic exposure to multiple pesticides may affect amphibian survival, growth and behavior (Hayes et al., 2006). Boone et al. (2005) found that larval amphibians exposed to both fertilizer and carbaryl together showed a decrease in survival, while each chemical tested individually did not impact survival. Results such as these illustrate the difficulty in predicting how pesticide interactions will impact survival or growth. This underscores the need for more in depth and detailed studies exploring pesticide and fertilizer mixtures in the laboratory and field settings.

5. Conclusions

We conducted a meta-analysis on globally important pesticides and fertilizers and found significant impacts on both survival and growth of amphibians. Understanding how different chemical classes of pesticides and fertilizers interact with amphibian populations can lead to new management practices and regulations. For example, in fields with amphibian communities, landowners could select pesticides from chemical classes that are less toxic to amphibians but still satisfy pest control needs. We suggest that agriculturalists work closely with extension specialists to identify products and information regarding wildlife impacts. Using an adaptive, integrated approach to pest management will enhance our ability to monitor and establish conservation efforts to help minimize amphibian population declines.

Conflict of interest

There is no conflict of interest.

Acknowledgments

We thank G. Paoletti, S. Bancroft, B. Hanshew, R. Hill, and M. Cook for helpful discussions and comments on the manuscript. We thank our funding sources, the Department of Fisheries and Wildlife at Oregon State University and the USDA Conservation Effects Assessment Project grant.

Appendix A. Results for the fixed effects model for survival (Table A.1) and growth (Table A.2) showing effect size and 95% bias corrected CI for the grand mean and each chemical class present in the analysis.

Table A.1
Fixed effects model results for the survival analysis organized by chemical class, effect size for each chemical class, and bias corrected 95% confidence intervals.

Chemical class	Effect size	Bias corrected 95% CI
Survival grand mean	−0.8731	−1.2166 to −0.5357
Carbamates	−0.2985	−0.7063 to −0.0571
Chlorophenoxy	0.0255	−0.1824 to 0.1435
Chloropyridinyl	−0.1279	−0.3567 to 0.0197
Inorganic	−0.6949	−1.4614 to −0.2535
Organochloride	−0.0653	−0.1233 to 0.0000
Organophosphorus	−0.4076	−1.0589 to −0.0717
Other	−0.0908	−0.2142 to 0.0099
Phosphonoglycine	−4.3596	−6.1193 to −2.6770
Pyrethroid	−0.0304	−0.1213 to 0.0259
Triazine	−0.7756	−2.8254 to −0.0069
Urea	0.0010	−0.0461 to 0.0345

Table A.2
Fixed effects model results for the growth analysis organized by chemical class, effect size for each chemical class, and bias corrected 95% confidence intervals.

Chemical class	Effect size	Bias corrected 95% CI
Growth grand mean	−0.0883	−0.1873 to −0.0081
Carbamates	0.0076	−0.1190 to 0.1751
Chloropyridinyl	0.1385	−0.0043 to 0.2966
Inorganic	−0.0311	−0.2284 to 0.1070
Organophosphorus	−0.3419	−0.6641 to −0.1784
Phosphonoglycine	−0.1032	−0.2547 to −0.0127
Pyrethroid	0.0566	−0.0484 to 0.3032
Triazine	−0.0264	−0.0971 to 0.0302

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