EcoHealth 11, 526–533, 2014
DOI: 10.1007/s10393-014-0944-9

ECOHEALTH

Original Contribution

Responses of Small Mammals to Habitat Fragmentation: Epidemiological Considerations for Rodent-Borne Hantaviruses in the Americas

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Abstract: Rodent-borne hantaviruses are a group of zoonotic agents that cause hemorrhagic fever in humans. The transmission of hantaviruses among rodent hosts may be higher with the increase of reservoir host abundance in a given area (density-dependent transmission) and with the decrease of small mammal diversity (dilution effect phenomenon). These population and community parameters may be modified by habitat fragmentation; however, studies that focus on fragmentation and its effect on hantavirus infection risk are scarce. To further understanding of this issue, we assessed some population and community responses of rodents that may increase the risk for hantavirus transmission among wildlife hosts in the Americas. We conducted a meta-analysis of published studies to assess the responses of small mammals to fragmentation of native habitats, relative to patch size. Our analyses included five countries and 14 case studies for abundance of reservoir hosts (8 species) and 15 case studies for species richness. We found that a reduction of patch area due to habitat fragmentation is associated with increased reservoir host abundances and decreased small mammal richness, which is mainly due to the loss of non-host small mammals. According to these results, habitat fragmentation in the Americas should be considered as an epidemiological risk factor for hantavirus transmission to humans. These findings are important to assess potential risk of infection when fragmentation of native habitats occurs.

Keywords: disease risk, emerging infectious diseases, meta-analysis, patch size effect, rodents, zoonosis

INTRODUCTION

Rodents, the most diverse order of mammals, are involved in the transmission of several zoonotic pathogens. In recent years, diseases caused by hantaviruses (family *Bunyaviridae*, genus *Hantavirus*) have emerged as some of the most important rodent-borne zoonoses (Jonsson et al. 2010). These globally widespread viruses are the etiological agents of hemorrhagic fever with renal syndrome in Eurasia (Old Word hantaviruses) and hantavirus pulmonary syndrome in the Americas (HPS; New World hantaviruses) (Jonsson et al. 2010). To date, more than 40 genotypes of hantaviruses have been reported in the Americas, from which 20

Electronic supplementary material: The online version of this article (doi:10.1007/s10393-014-0944-9) contains supplementary material, which is available to authorized users.

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are associated with diseases in humans (Hjelle and Torres-Pérez 2010).

The expansion of human activities at expenses of natural environments (deforestation, agriculture, urbanization, etc.) may result in changes in hantavirus infection dynamics, sometimes creating conditions for the emergence of rodent-borne hemorrhagic fevers (e.g., Lee et al. 1980; Zeitz et al. 1995; Yahnke et al. 2001; Ruedas et al. 2004; Dearing and Dizney 2010). The change of rodent community structure in human-dominated landscapes could be an important driver of these outbreaks, mainly because of two factors: (1) the increase of reservoir host abundance, as there is evidence that several hantaviruses are horizontally transmitted in a density-dependent manner (Niklasson et al. 1995; Mills et al. 1999; Madhav et al. 2007); and (2) the decrease of small mammal diversity, as hantaviruses may increase their infection prevalence in rodent hosts inhabiting species-poor communities, a phenomenon called dilution effect (Keesing et al. 2006). This phenomenon, originally described for vector-borne pathogens (Keesing et al. 2006), is suggested to occur in some Old World and New World hantaviruses such as Choclo virus, Puumala virus, and Sin Nombre virus (Tersago et al. 2008; Clay et al. 2009; Dizney and Ruedas 2009; Suzán et al. 2009; Carver et al. 2011a; Voutilainen et al. 2012). Furthermore, both driving factors could operate synergistically to influence disease transmission among hosts.

Habitat fragmentation is a worldwide phenomenon that modifies the composition and structure of communities (Fahrig 2003). Frequently, habitat fragmentation tends to simplify communities: whereas generalist species (those that have a high adaptability to a wide range of habitats and food sources) become dominant, specialist species tend to reduce their abundance and richness (Ewers and Didham 2006). However, this pattern does not always occur (Fahrig 2003). Because the most competent hosts of hantaviruses are expected to have generalist habits (Dearing and Dizney 2010), habitat fragmentation should increase the abundance of reservoir hosts. Consequently, and in agreement with the dilution effect hypothesis and the density-dependent transmission, hantavirus prevalence in reservoir hosts should increase in fragmented landscapes. However, in spite of the wide geographic distribution of different hantaviruses in the Americas and the widely distributed phenomenon of habitat fragmentation, very few studies have empirically analyzed the relationships between fragmentation and hantavirus prevalence and/or population and community parameters of small mammals that may influence hantavirus dynamics. In two studies, fragmentation increased hantavirus (Sin Nombre virus) prevalence in the reservoir host (*Peromyscus maniculatus*) in North America (Langlois et al. 2001; Mackelprang et al. 2001). In another study, the abundance of *Oligoryzomys fulvescens* and *Zygodontomys brevicauda* (reservoir hosts of Choclo and Calabazo virus) increased (while the diversity of small mammals decreased) at the edge of tropical forest fragments in Panama (Suzán et al. 2008). Further information is needed to establish the direction, strength, and generalization of the relationships between habitat fragmentation and the risk of hantavirus infection in the Americas.

In this study, we assessed the general effect of habitat fragmentation on species richness of the rodent communities, and population abundance of reservoir hosts that are involved in hantavirus dynamics. We hypothesized that fragmentation of native habitats is associated with a reduction in species richness and an increase in the abundance of hantavirus reservoirs. To test this hypothesis, we conducted a meta-analysis of published studies concerning the responses of non-volant small mammals (rodents and marsupials) to habitat fragmentation in the Americas. We discussed the potential implications of our findings in relation to the epidemiological risk for hantavirus transmission to humans.

METHODS

Data Collection

We searched scientific publications in the Web of Science and Scopus databases to track original research articles focused on small mammal assemblages in fragmented habitats, published from 1985 to 2012. We used a combination of key words: "fragmentation*," "small mammal*," "rodent*," and the genus names of hantavirus reservoirs in the Americas according to Jonsson et al. (2010). Articles included could either report on observational or experimental studies. We evaluated the effects of fragmentation of native habitats relative to patch size, not relative to edge effects or the degree of isolation (e.g., Markl et al. 2012; Vargas et al. 2012). Therefore, articles included in the analysis had to report comparisons of native fragment remnants of different sizes or comparisons of native fragments versus continuous native habitats. If a study made paired comparisons of patch sizes separately (e.g., small vs. large and medium vs. large patches), we only used the outcomes resultant from the comparisons between the smallest and the largest patches (Markl et al. 2012). Then, the following information was recorded for each reference: (1) abundance of reservoir hosts (at species level); (2) abundance of small mammal species that are not hantavirus reservoirs (non-host, hereafter); (3) species richness (cumulative number of small mammal species); (4) original biome at the study area (e.g., Mediterranean ecosystems, temperate forests, tropical forests, deserts, etc.); (5) sample size; and (6) statistical results, if possible. Non-host small mammals were considered the species belonging to genera that are not reported as hantavirus reservoir hosts by Jonsson et al. (2010); data for non-host species were included only in articles that had at least one reservoir host. If there was more than one article with the same study area, we selected the one that had a larger sample size, and/or a longer sampling period. Each comparison was considered an independent case study and articles might be comprised of more than one comparison. For example, whenever there was more than one reservoir species in the same study, each of them was considered an independent case study.

Data Analysis

To measure whether there was a pattern (increase or decrease) of change in abundance and species richness in response to habitat fragmentation (patch size reduction), we calculated the effect sizes (ESs) to perform the meta-analysis. Correlation coefficient r was calculated for each entry in the database, which we then converted into Fisher's z transform, a measure of ES (Rosenberg et al. 2000). When a study did not report a correlation coefficient, we estimated r from other statistical data such as F, t, and P (Rosenberg et al. 2000), or from raw data when articles included them. Confidence intervals (CIs) of ES were estimated from the ES and their variances through bootstrap re-sampling procedures (999 iterations) (Rosenberg et al. 2000), using random-effect models as we assumed ES varied randomly among comparisons (Gurevitch and Hedges 2001). A negative ES indicates that abundance or richness decrease with fragmentation, while positive ES indicates that abundance or richness increase with fragmentation.

Data were grouped into categories (e.g., climate, genera, species) to detect patterns in the response to fragmentation depending on ecological or taxonomic attributes. We only performed comparisons when sample size of ESs were ≥ 5 in each group. Heterogeneity of ES within and between groups was examined with Q statistics (Hedges and Olkin 1985). This test is analogous to an ANOVA, testing whether the variance of ES is greater than expected by chance alone (Rosenberg et al. 2000).

As a complement to the ES analysis of species richness, we used two-proportion Z test to compare the proportion of reservoir hosts (plus species that belong to the same genus) and non-host species that were absent in either small fragments or continuous habitat (or larger fragments). In case the meta-analysis showed that species richness decreased in smaller fragments, we identified which species were lost in small fragments, but that were present in large fragments or continuous habitat. In case richness increased in small fragments, we identified which species were absent in large fragments or continuous habitat.

We considered the possibility of publication bias because the probability of publication of a given study increases if it reports significant results (Arnqvist and Wooster 1995). Publication bias was assessed through Kendall's Tau and Spearman rank correlation tests (Rosenberg et al. 2000). In addition, we used the Rosenthal fail-safe method to estimate the number of null results that would need to be added to the meta-analysis to nullify its overall ES (Rosenthal 1979). All meta-analyses were performed in the meta-analytic software MetaWin version 2.0 (Rosenberg et al. 2000).

RESULTS

Our final database included 19 papers reporting quantitative information satisfying our criteria for the meta-analysis (see Supplementary material, Appendix S1), and they included studies conducted in five countries (Brazil, Chile, Canada, USA, and Venezuela). Thirteen papers were used for the analysis of reservoir host abundance (including eight species) and seven papers for non-host species. From these articles, 14 independent case studies were analyzed for abundance of reservoir hosts (Table 1) and 30 for non-host species (see Supplementary material, Appendix S2). Fourteen papers were used for the analysis of species richness, comprising 15 independent case studies. Ten articles reported data on species that disappeared in small fragments.

We found that a reduction of habitat patch size by habitat fragmentation had a significant positive effect in the overall ES for abundance of reservoir hosts, with an average

Table 1. Hantavirus reservoir hosts analyzed in this study, and their respective hantavirus strain and distribution, according to Jonsson et al. 2010

Hantavirus reservoir hosts	Country of study	Number of cases	Hantavirus strain	Geographic distribution of virus
Akodon montensis	Brazil	1	Ape Aime virus, Jaborá virus, Juquitiba-like virus*	Brazil, Paraguay
Microtus pennsylvanicus	USA	1	Prospect Hill virus	Maryland
Oligoryzomys longicaudatus	Chile	1	Andes virus*, Oran virus*	Argentina and Chile
Oligoryzomys nigripes	Brazil	1	Itapúa virus, Juquitiba virus*, Juquitiba-like virus*	Brazil, Paraguay
Peromyscus leucopus	USA	3	Monongahela virus*, New York virus*	North America
Peromyscus maniculatus	Canada, USA	3	Sin Nombre virus*	North America
Rattus rattus	Chile, USA	3	Gou virus, Seoul virus*	China, Worldwide
Zygodontomys brevicauda	Venezuela	1	Calabazo virus	Panama

* Hantavirus strains known to produce disease in humans.

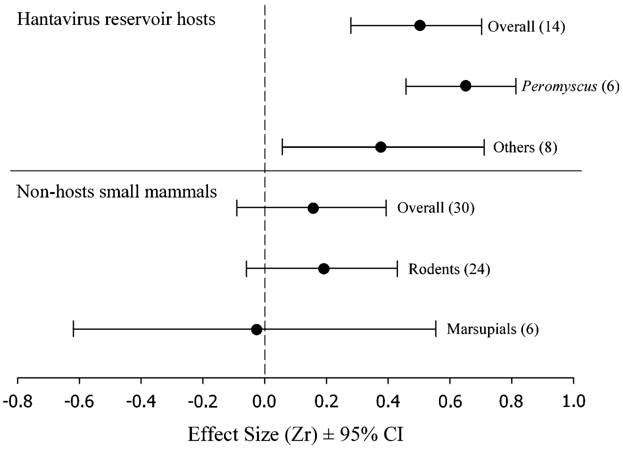

Figure 1. Effect sizes ±95% CI of small mammal abundances (hantavirus reservoir host and non-host small mammals) associated with patch size reduction. Sample size of effect sizes are shown in parentheses. The *vertical dashed line* indicates the 0 value. Effects are statistically significant when the 95% CI of effect sizes do not overlap with 0.

ES of 0.51 (IC 0.29–0.70) (Fig. 1). Only the species of the genus *Peromyscus* (*Peromyscus leucopus* and *P. maniculatus*) had a sample size $\geq$5; therefore, two groups were formed: *Peromyscus* species and the rest of reservoir species. Habitat fragmentation had a significant positive effect for both groups (Fig. 1), and the groups did not differ significantly in their response to fragmentation ($Q_{\text{within}} = 12$; $P = 0.44$; $Q_{\text{between}} = 1.9$; $P = 0.17$). In contrast, abundance of non-host species did not present a significant effect, either for the overall ES or in separate groups (rodents or marsupials) (Fig. 1). Groups did not differ in heterogeneity of ES ($Q_{\text{within}} = 25.9$; $P = 0.6$; $Q_{\text{between}} = 0.4$; $P = 0.5$).

Habitat fragmentation had a significant negative effect on total species richness, with an average ES of −0.46 (IC −0.72 to −0.20) (Fig. 2). Only rodent communities in tropical forests had a sample size $\geq$5; therefore, two groups were formed: tropical forests and all other biomes (Mediterranean ecosystems, temperate forests, and boreal forests). Both groups had a significant negative response to habitat fragmentation (Fig. 2). No significant heterogeneity was found between ES of groups ($Q_{\text{within}} = 13.7$; $P = 0.4$; $Q_{\text{between}} = 0.002$; $P = 0.97$). The decrease of species richness in small fragments is mainly due to the loss of non-host small mammals, as 78% of species expected in the

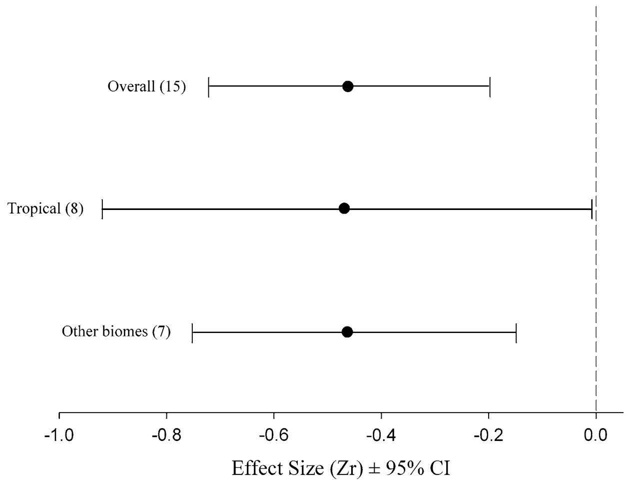

Figure 2. Effect sizes ±95% CI of small mammal richness associated with patch size reduction. Sample size of effect sizes are shown in parentheses. "Other biomes" include Mediterranean ecosystem ($n = 3$), temperate forest ($n = 2$), and boreal forest ($n = 2$). The interpretation of graph is the same as found in Fig. 1.

habitat that were absent in small fragments were non-host species ($n = 37$; $Z = 3.45$; $P < 0.001$).

No publication bias was detected in data used on the assessment of overall ES, either for reservoir host abundance (Kendall's Tau = 0.19; $P = 0.34$; Spearman $R_s = 0.27$; $P = 0.36$) or small mammal richness (Kendall's Tau = −0.05; $P = 0.80$; Spearman $R_s = -0.04$; $P = 0.88$). Rosenthal's fail-safe numbers also suggested no bias among study cases. Under this criterion, at least 146 non-significant study cases for reservoir host abundance, and 145 for species richness would need to be added to the analysis to change results from significant to nonsignificant.

DISCUSSION

The meta-analysis showed that there were significant changes in reservoir host abundances (positive ES) and total species richness (negative ES) associated with fragmentation of native habitats, in agreement with our hypothesis. The results of publication bias analyses suggest that the above results were not the result of publication bias. According to the model of density-dependent transmission, an increase in the abundance of hosts associated with fragmentation should increase the risk of hantavirus transmission, given that it may increase interactions among reservoir hosts, resulting in an increase of infected animals (Dobson and Hudson 1995; Begon et al. 2002). Several studies have provided evidence supporting a positive relationship between host density and hantavirus infection prevalence (e.g., Niklasson et al. 1995; Escutenaire et al. 1997; Olsson et al. 2002). In the Americas, this finding have been reported particularly for Sin Nombre virus, including the delayed density-dependence phenomenon (Mills et al. 1999; Yates et al. 2002; Madhav et al. 2007; Carver et al. 2011b), which is a time lag between increases in population density and increases in infection prevalence in host populations. However, because some studies have reported no relationship or an inverse relationship between host densities and hantavirus prevalence (Boone et al. 1998; Abbott et al. 1999; Douglass et al. 2001), the density-dependence transmission in hantavirus is not a clear pattern.

Some of the species analyzed here are involved in the transmission of hantaviruses that cause diseases of concern for humans. For example, *P. leucopus* and *P. maniculatus* are implicated in the transmission of three hantaviruses that cause HPS in North America (Table 1). Other important reservoir hosts included in the analysis were *Akodon montensis*, *Oligoryzomys longicaudatus*, and *Oligoryzomys nigripes*, which transmit hantaviruses that cause HPS in Argentina, Chile, and Brazil (Table 1). The invasive *Rattus rattus* is another hantavirus reservoir host that has relevance for public health due to the several zoonotic diseases that it can transmit, such as the worldwide-distributed Seoul virus (Wang et al. 2000). There are reports of *R. rattus* infected with New World hantaviruses, including Andes virus (Lobos et al. 2005), which might increase the epidemiological risk associated with this species.

Regarding non-host small mammals, we did not find any significant patterns, which may be a consequence of the broad range of ecological traits associated with species included in this group. However, when species richness decreases in response to fragmentation, the non-host species are the ones that tend to disappear as fragment size decreases. Therefore, a decrease in species diversity may increase the probability of hantavirus transmission among individual hosts (Tersago et al. 2008; Clay et al. 2009; Suzán et al. 2009; Carver et al. 2011a), in agreement with the dilution effect hypothesis (Keesing et al. 2006; Ostfeld and Keesing 2012). The increase in reservoir host abundance and the decrease in species richness may act synergistically to increase prevalence in rodent hosts, in turn increasing the threat of transmission to humans.

Assessing general patterns of small mammal communities by using approaches such as meta-analysis produces valuable information for understanding the effects of human disturbances on the dynamics of prevalence in host species and potential pathogen transmission. Although this study only addressed one component of habitat fragmentation, other features associated with fragmented landscapes such as degree of isolation between patches, edge effect, and matrix composition, have important consequences for the structure of wildlife communities (Pardini 2004; Debinski 2006; Prugh et al. 2008; Brady et al. 2011). Therefore, these variables may also influence the transmission dynamics and risk of hantavirus infection in humans (Suzán et al. 2012). Further studies should verify if the increase of reservoir host abundance and decrease of small mammal diversity due to habitat fragmentation result in an increase of hantavirus infection prevalence in reservoir hosts in different geographic regions.

Recently, new geographic locations of hantavirus detection and novel hantaviruses are being described in the Americas (Cruz et al. 2012; Kariwa et al. 2012; Matheus et al. 2012) and in other parts of the world (Blasdell et al. 2011; Zhang et al. 2011; Guo et al. 2013). Because changes in natural environments due to human activities will continue occurring on a large scale, modifying biodiversity composition (Brooks et al. 2002; Myers et al. 2013), and because contrasting results have been reported on the effects of human disturbance on hantavirus dynamics (Dearing and Dizney 2010), more investigation is necessary to understand the relationships between hantaviruses, their hosts, and the environment.

CONCLUSION

In conclusion, the increase in reservoir host abundance and the decrease in small mammal richness are general patterns associated with habitat fragmentation in several areas in the Americas. Our findings support the claim that habitat fragmentation has the potential to increase epidemiological risk of hantavirus transmission among hosts in the Americas, under the assumptions that hantavirus transmission is generally influenced by the abundance of reservoir hosts (density-dependence transmission) and/or the diversity of small mammal communities per se (the dilution effect phenomenon). Despite the study's limitation of including data for only eight reservoir species of hantaviruses, some of the included species are of epidemiological importance because they are known to transmit relevant hantavirus strains to humans. To our knowledge, this is the first meta-analysis that addresses the responses of small mammals to habitat fragmentation applied to epidemiological risk assessments. Given that the effects of human disturbance on wildlife communities can modify the dynamics of zoonotic diseases in reservoir hosts, our results are important to consider in assessing disease risk resulting from fragmentation of native habitats.

ACKNOWLEDGMENTS

We thank the Disease Ecology Group (FMVZ, UNAM), Gerardo Ceballos, Rurik List, Catherine Machalaba, and two anonymous reviewers for comments and suggestions that improved this manuscript, and the Postgraduate Program (FMVZ, UNAM) for support. We are grateful to Carolyn Brown and Kendra Shannon (UNAM-Canada) for reviewing the English of an early version of this manuscript. A.V. Rubio is supported by a CONICYT Becas-Chile Scholarship.

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