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In My Opinion

Phylogenetic Patterns Suggest Broad Susceptibility to Chronic Wasting Disease Across Cervidae

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ABSTRACT Chronic wasting disease presents significant management challenges for North American species of Cervidae, but susceptibility of other cervid taxa worldwide to this disease is largely unknown. A review of 7 published partial phylogenies for Cervidae indicates that known susceptible taxa are broadly distributed across each of these phylogenies, suggesting that there may be broad susceptibility to the disease within the family. Taxa particularly at risk based on phylogenetic and geographic proximity to known susceptible species include species of the genus *Mazama* in Central and South America and species of the genera *Cervus* and *Rusa* in Europe and Asia. © 2020 The Wildlife Society.

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Chronic wasting disease (CWD) is an invariably fatal neurodegenerative disease affecting multiple species in the family Cervidae (Mammalia: Artiodactyla; Williams et al. 2002, Miller and Williams 2004). Certain species of Cervidae are managed for subsistence harvest, recreational hunting, and wildlife-watching (Wallmo 1981, Halls 1984, Toweill 2002, Franzmann and Schwartz 2007, Hewitt 2011), while other species in the family are considered rare and potentially at-risk for extinction (Duarte et al. 2008, Heckeberg et al. 2016). Chronic wasting disease generally is acknowledged to be a significant concern for the management of certain cervid species, including North American deer (*Odocoileus* spp.), elk or wapiti (*Cervus canadensis*), and moose (*Alces alces*; Edmunds et al. 2016, Gillin and Mawdsley 2018).

Chronic wasting disease is a transmissible spongiform encephalopathy (TSE), similar to bovine spongiform encephalopathy in cattle, scrapie in sheep, and Creutzfeldt-Jakob disease in humans (Travis and Miller 2003). The TSEs are caused by misfolded prion proteins that accumulate in lymphoid and nervous system tissues, leading to cell death, neurological impairment, and mortality (Miller et al. 2006). In CWD, infected animals shed misfolded prions into the environment, where the prions can remain infectious for many years (Miller and Williams 2004). There are no treatments or vaccines for CWD (Wood et al. 2018).

To date, reported cases of CWD are confined to wild and captive cervid populations of several species in North America, South Korea (as a result of importation of infected live animals from North America), Finland, and Norway (Gillin and Mawdsley 2018). Concerns exist about possible introduction of the disease to novel host species and populations worldwide, especially given the global transport and trade in live cervids (which led to the introduction of the disease in South Korea) and the trade in cervid products such as meat, antler velvet, and urine (which could potentially also transport infectious prions [Gillin and Mawdsley 2018]). Experimental evidence indicates that other species in the family Cervidae are susceptible to CWD in addition to those taxa in which the disease has been detected in the wild (e.g., Balachandran et al. 2010, Hamir et al. 2010, Nalls et al. 2013).

Phylogenetic inference provides an additional set of approaches for estimating susceptibility of wildlife species to novel diseases. Such methods infer disease response in species for which susceptibility is unknown based on phylogenetic proximity to other species with known disease response (Burbrink et al. 2017). These inferential methods build on the commonplace observation that many animal diseases are restricted to certain clades or taxonomic groups.

Burbrink et al. (2017) used a phylogenetic approach to estimate susceptibility of North American snake taxa to snake fungal disease. These authors found that individual taxa with known susceptibility to snake fungal disease were widely distributed across the published phylogenetic trees for North American snakes. Based on the lack of phylogenetic clustering of the species with known susceptibility to snake fungal disease, these authors concluded that additional North American snake taxa likely would be expected to exhibit susceptibility to this disease (Burbrink et al. 2017). Other well-known examples of wildlife diseases that

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are associated with particular clades include rabies in mammals, feline leukopenia in cats, canine parvovirus in dogs, white-nose syndrome in bats, and amphibian chytrid fungus in frogs.

Application of a similar approach to estimate susceptibility of species of Cervidae to CWD is promising, but is complicated by multiple factors including the lack of a phylogenetic hypothesis that includes all known taxa; lack of agreement on the taxonomic status of certain species and subspecies; and significant lack of agreement regarding the phylogenetic patterns of relationships for certain taxa in the multiple partial phylogenies of this family that have been published to date (Heckeberg et al. 2016). Phylogenetic estimation of CWD susceptibility within Cervidae is a less complex analytical problem than estimation of susceptibility of snakes in eastern North America to snake fungal disease, given the smaller number of taxa involved. The total number of species of Cervidae worldwide (55; Heckeberg et al. 2016) is smaller than the total number of snake taxa in eastern North America (98; Burbrink et al. 2017). We currently have CWD susceptibility information for just 9 of the 55 cervid species (Gillin and Mawdsley 2018). With this smaller number of taxa, well-known descriptive phylogenetic statistics such as the consistency index and retention index (Farris 1989) can be applied to provide an initial estimate of the degree to which CWD susceptibility is clustered on the phylogeny of Cervidae.

METHODS

For this analysis, I used 3 complementary approaches to examine whether there may be a phylogenetic constraint on CWD susceptibility within Cervidae. All rely on the standard phylogenetic modeling procedure of "mapping" a feature, such as known CWD susceptibility, as a "character" onto the available phylogenies for the family (Lipscomb 1998). The first approach measures the number of independent derivations of this character. Following the arguments of Burbrink et al. (2017), fewer or no independent derivations would indicate phylogenetic clustering of the character in a particular lineage, suggesting the possible presence of a phylogenetic constraint; multiple derivations would suggest a lower degree or absence of phylogenetic constraint. The second approach uses the consistency index of Farris (1989) to compare the number of observed derivations for the character relative to the minimum possible number of such derivation. Higher values of the consistency index indicate greater congruence between the character and the phylogeny and, therefore, a greater degree of phylogenetic constraint (Lipscomb 1998). The third approach uses the retention index of Farris (1989) to measure the degree to which the distribution of the character reflects patterns of grouping in the phylogeny. Higher values of the retention index indicate a greater degree of phylogenetic clustering of the character in question and, therefore, a greater degree of phylogenetic constraint. Values of the consistency index and retention index both range from 0 to 100 (Farris 1989, Lipscomb 1998). Together, these 3 approaches provide an initial estimation of the degree to which CWD susceptibility may be phylogenetically constrained within Cervidae.

As noted above, there are several published partial phylogenies of Cervidae, which differ in the taxa included, the sequence or other input data used, analytical methods applied, and patterns of phylogenetic relationships recovered. I mapped known CWD susceptibility as a character onto 7 published phylogenies cited by Heckeberg et al. (2016; Table 1). Heckeberg et al. (2016) is the most comprehensive of the published phylogenetic trees and was recreated to illustrate both the phylogenetic position of taxa with known CWD susceptibility as well as the phylogenetic position of cervid taxa on the International Union for the Conservation of Nature (IUCN) Red List (Fig. 1).

RESULTS

In each of the 7 published phylogenies, taxa with known susceptibility to CWD are distributed across the phylogeny and do not form a monophyletic group, requiring either n-1 or n-2 steps (where n is the number of taxa with known CWD susceptibility). This lack of cladistic grouping also is evident in the low reported values for the consistency index (average value of 16.16 across all studies) and retention index (average value of 24.76 across all studies; Table 1).

DISCUSSION

In each of the 7 reviewed phylogenies, mapping CWD as a character yielded low values of the consistency index and

Table 1. Chronic wasting disease (CWD) susceptibility mapped as a character to 7 published phylogenies of Cervidae: number of steps, consistency index, and retention index.

Published cervid phylogeny	No. of known CWD-susceptible taxa[a]	No. of steps[b]	Consistency index[c]	Retention index[c]
Pitra et al. (2004)	8	7	14.29	16.67
Fernandez and Vrba (2005)	8	6	16.67	40.00
Gilbert et al. (2006)	8	7	14.29	16.67
Agnarsson and May-Collado (2008)	8	7	14.29	16.67
Hassanin et al. (2011)	8	7	14.29	16.67
Zhang and Zhang (2012)	5	4	25.00	33.33
Heckeberg et al. (2016)	9	7	14.29	33.33

[a] As per Gillin and Mawdsley (2018).
[b] Calculated as per Lipscomb (1998).
[c] As defined by Farris (1989).

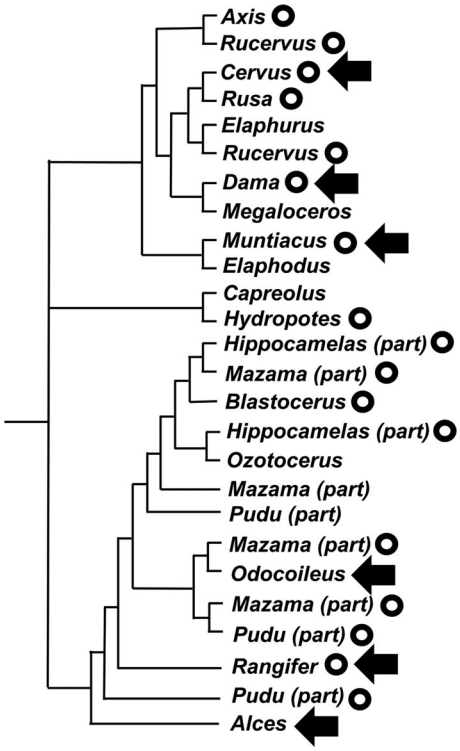

Figure 1. Phylogenetic relationships among genera of Cervidae, redrawn from Heckeberg et al. (2016). Genera containing ≥1 species with known susceptibility to chronic wasting disease (CWD) are indicated by solid arrows; genera containing ≥1 species on the International Union for Conservation of Nature Red List are indicated by open circles. Three genera, *Mazama, Pudu,* and *Hippocamelas,* are polyphyletic in the phylogeny of Heckeberg et al. (2016).

retention index, indicating a consistent lack of phylogenetic grouping of the CWD-susceptible taxa within these 7 published phylogenies of Cervidae. These consistent findings across published phylogenies suggest that susceptibility to CWD is probably not phylogenetically constrained within Cervidae. Following the arguments advanced by Burbrink et al. (2017), additional species within this family are likely susceptible to the causative agent of the disease. In the 7 published phylogenetic studies, the CWD-susceptible species never form a distinct monophyletic group and are widely separated and dispersed across the published phylogenetic trees. In all cases, the minimum-sized monophyletic group that would include all of the known CWD-susceptible species is coextensive with the family Cervidae. Taken together, these findings suggest that there may be broad susceptibility to CWD across the entire family Cervidae.

Published phylogenies also can be used to estimate which of the other taxa within Cervidae are at greatest risk for acquiring CWD, again based on the phylogenetic proximity of taxa with unknown susceptibility to CWD to taxa with known susceptibility. In the phylogeny of Heckeberg et al. (2016), the 2 North American deer in the genus *Odocoileus* (both of which are highly susceptible to CWD; Williams et al. 2002) nest within a larger clade consisting of Central and South American species of the brocket deer genus *Mazama*. This latter clade includes 5 species considered to be at elevated risk of extinction by the IUCN, and whose geographic distributions overlap those of ≥1 *Odocoileus* species (Allen 1915, Duarte et al. 2008, Abril et al. 2010). Based on phylogenetic proximity and the geographic overlap with species having known susceptibility to CWD, these *Mazama* species may be at elevated risk for CWD transmission, and every effort should be made to prevent the introduction of CWD into areas occupied by these deer species. Likewise, *C. canadensis,* a species highly susceptible to CWD, nests within a larger clade containing species of the genera *Cervus* and *Rusa* (Heckeberg et al. 2016). This larger clade contains 5 species in these 2 genera that are considered to be at elevated risk of extinction by the IUCN. As with the species of *Mazama,* these species of *Cervus* and *Rusa* also may be at elevated risk for CWD transmission; therefore, every effort should be taken to prevent the introduction of CWD into areas occupied by these species.

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