

Impacts of a Global Climate Cycle on Population Dynamics of a Migratory Songbird

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Progress toward understanding factors that limit abundances of migratory birds, including climate change, has been difficult because these species move between diverse locations, often on different continents. For black-throated blue warblers (*Dendroica caerulescens*), demographic rates in both tropical winter quarters and north temperate breeding grounds varied with fluctuations in the El Niño Southern Oscillation. Adult survival and fecundity were lower in El Niño years and higher in La Niña years. Fecundity, in turn, was positively correlated with subsequent recruitment of new individuals into winter and breeding populations. These findings demonstrate that migratory birds can be affected by shifts in global climate patterns and emphasize the need to know how events throughout the annual cycle interact to determine population size.

The need to understand when and how bird populations are limited is made pressing by recent declines in the abundances of many species, especially migratory songbirds (1). Quantifying the effect and timing of limiting factors for migratory species, however, is difficult because the birds spend different parts of their annual cycle in different locations. Furthermore, events during one stage of the annual cycle are likely to influence populations in subsequent stages (2). Here we show through long-term demographic studies of a migratory songbird that the El Niño Southern Oscillation (ENSO) impacts demographic rates in both the breeding and nonbreeding seasons. Our findings also reveal links in the population dynamics of this species between stages of its annual cycle.

We measured the effect of ENSO on survival, fecundity, and recruitment of the black-throated blue warbler, a migratory songbird that breeds in forested regions of eastern North America and overwinters primarily in the Greater Antilles. This species is territorial, largely insectivorous, and exhibits strong site fidelity in both its breeding and wintering grounds (3). We quantified warbler demography from 1986 to 1998 at two locations during the annual cycle: the overwinter period at Cope Mountain, near Bethel Town in northwestern Jamaica, West Indies, and the breeding season at Hubbard Brook Experimental Forest, West Thornton, New Hampshire, USA. The species' habitat at both sites was mature mesic forest, relatively undisturbed by human activity. Demographic data were collected annually

from the overwintering population in late October and from the breeding population in mid-May through August. For all analyses, we used annual mean monthly values of the standardized Southern Oscillation Index (SOI) to represent ENSO conditions for each calendar year (4). High, positive values of SOI indicate La Niña conditions and low, negative values indicate El Niño conditions (5).

Annual survival (6) of black-throated blue warblers in Jamaica (Fig. 1, A to B) was strongly associated with SOI: survival was low in El

Niño years and high in La Niña years (Fig. 2). This result is best explained by the impact of ENSO on local climate and a concomitant change in food availability for overwintering birds. In the winter dry season, migrant songbirds are often food-limited (7) and can be in a state of physiological decline (8), especially in late winter before spring migration. During El Niño years in Jamaica, reduced rainfall (9) probably leads to a decreased amount of food available for warblers in the winter dry season and, hence, to lower survival. La Niña years, in contrast, tend to be wetter and thus would result in increased food availability and higher survival.

Annual survival of warblers breeding in New Hampshire (Fig. 1, C to D) was relatively constant and did not consistently fluctuate with changes in ENSO (Fig. 2). Breeding populations of black-throated blue warblers mix extensively on their Caribbean winter quarters (10), and these islands vary in the extent to which they are affected by ENSO (9, 11). Thus, the lack of association between annual survival in New Hampshire and SOI is probably due to many individuals in the breeding population overwintering on other islands, particularly Cuba (12), where the climatic effects of ENSO can be less severe compared with Jamaica (9, 13).

ENSO had significant effects on warbler fecundity in New Hampshire. We measured two components of fecundity (14): (i) number of offspring fledged and (ii) mass at fledging, a

Fig. 1. Chronology of major demographic events in relation to a given ENSO year. The x axis delimits a 24-month period over two concurrent calendar years. "Year 1" is the ENSO year being considered. ENSO phase (open bar) is represented by the mean of Year 1's monthly values of the standardized SOI. Closed bars symbolize overwinter (black) and breeding (gray) periods for warbler populations; thick portions show when birds were present at the respective locations. Letters along the black and gray bars indicate timing of warbler capture and recapture used in survivorship analyses. For example, A to B represents annual (October–October) survivorship in Jamaica. Arrows linking the breeding and overwintering populations signify warbler migration and recruitment (1, autumn migration; 2, spring migration).

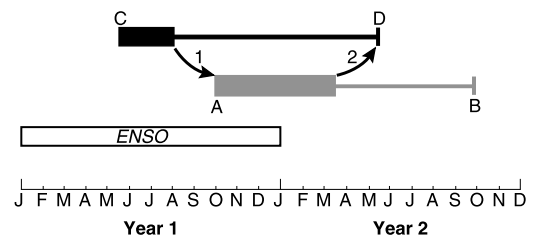
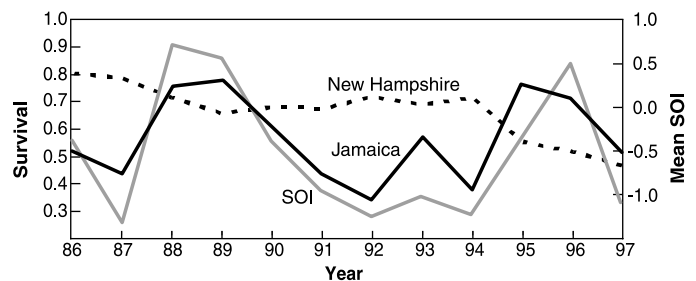


Fig. 2. Comparison of annual survival estimates (37) for black-throated blue warblers in Jamaica (black line) and New Hampshire (dashed line) to mean monthly values of SOI (gray line). X axis represents capture year for survival curves and ENSO calendar year for SOI curve. Left y axis gives estimated warbler survival to the next calendar year. Right y axis indicates mean monthly values of SOI. Based on capture-mark-recapture analyses (37), annual survival probability in Jamaica from year, to year, ₊₁ was a linear function of mean monthly SOI in year; annual survival probability in New Hampshire was constant among years. Recapture probability was constant among years in both locations (0.95 in Jamaica; 0.86 in New Hampshire).



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REPORTS

general predictor of offspring survival (15). Mean number of young fledged per warbler pair was weakly correlated (16) with SOI ($r = 0.39$, $P = 0.18$). However, mass at fledging was highly correlated with SOI: fledglings weighed less in El Niño years relative to La Niña years (Fig. 3A). After accounting for variation in fledgling mass and hence its expected effect on survival (17), annual fecundity was correlated with SOI (Fig. 3B).

Because black-throated blue warbler fecundity is limited by food availability (18), we tested if variation in availability of lepidopteran larvae, the warbler's primary prey in summer, was related to ENSO. Food is most limited from mid-June to mid-July when adults are feeding nestlings and dependent juveniles. At the New Hampshire site, total larval biomass recorded annually on mid-June through mid-July censuses (19) was positively correlated with annual fecundity ($r = 0.58$, $P < 0.05$) and with SOI ($r = 0.58$, $P < 0.04$). Prey biomass was low during El Niño years and high during La Niña years. These results suggest that ENSO influences fecundity of black-throated blue warblers by affecting their food supply.

The effects of ENSO on warbler fecundity had consequences for demography in subsequent seasons (20). First, the number of juveniles at the Jamaica site each October (i.e., recruitment to the overwintering population; see arrow "1" in Fig. 1) was positively correlated with SOI ($r = 0.71$, $P < 0.007$) and with

fecundity from the preceding summer in New Hampshire (Fig. 4A). Second, the number of yearling breeders each May in New Hampshire (i.e., recruitment of the preceding year's fledglings into the breeding population; see arrow "2" in Fig. 1) was positively correlated with both warbler fecundity (Fig. 4B) and mean monthly SOI ($r = 0.59$, $P < 0.04$) from the previous year. In both Jamaica and New Hampshire, low annual recruitment of both juveniles and yearlings was associated with El Niño conditions, whereas high recruitment was associated with La Niña events.

ENSO has been shown to impact demographic rates and food resources of many animal taxa, including seabirds (21), raptors (22), Pacific island passerines (23), primates and rodents (24), and arthropods (25). The results presented here provide evidence that ENSO, through its effect on food supply, limits survival, fecundity, and recruitment of a migratory songbird. Additionally, they illustrate an important interaction between summer and winter population dynamics that operates through a common link to the ENSO cycle. Populations of migratory birds are therefore susceptible over a range of spatial and temporal scales to shifts in global climate patterns.

Evidence is accumulating that bird populations are being affected by global warming associated with long-term climate change (26).

Global warming could also be increasing the severity of ENSO events (27). If this is true, we predict that variance in demographic rates of migratory bird populations will become amplified, leading to elevated extinction risk, especially for small populations (28). Because many migratory bird species are declining in abundance and therefore of conservation concern, field research and demographic modeling efforts should focus on understanding how events throughout the annual cycle are interconnected and on how multiple limiting factors, both natural and human-related, determine population size.

References and Notes

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14. We documented the fate of all nests found and recorded the number of young fledged annually per warbler pair ($n = 488$ pairs) within a 64-ha plot in New Hampshire. All nestlings were weighed and banded on day 6 after hatching, the last day to safely handle young during the 8-day nestling period without causing premature fledging. Therefore, the mass on day 6 was used as the estimate of mass at fledging. Annual mean fledgling mass was computed by first averaging mass on a per nest basis ($n = 392$ nests) and then averaging means for all nests per year.
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16. We conducted Durbin-Watson tests for independence for all correlation analyses and found no statistical evidence of temporal autocorrelation.
17. Because heavy fledglings were likely to have higher survival rates than lighter fledglings (15), we used the ratio of mean fledgling mass to the maximum fledgling mass for all years (1988) as an index of offspring survival (e.g., survival index for 1995 = mean fledgling mass₁₉₉₅/mean fledgling mass₁₉₈₈). We multiplied the mean number of fledglings by the survival index to calculate annual warbler fecundity (e.g., fecundity for 1995 = mean number fledged₁₉₉₅ · survival index₁₉₉₅).
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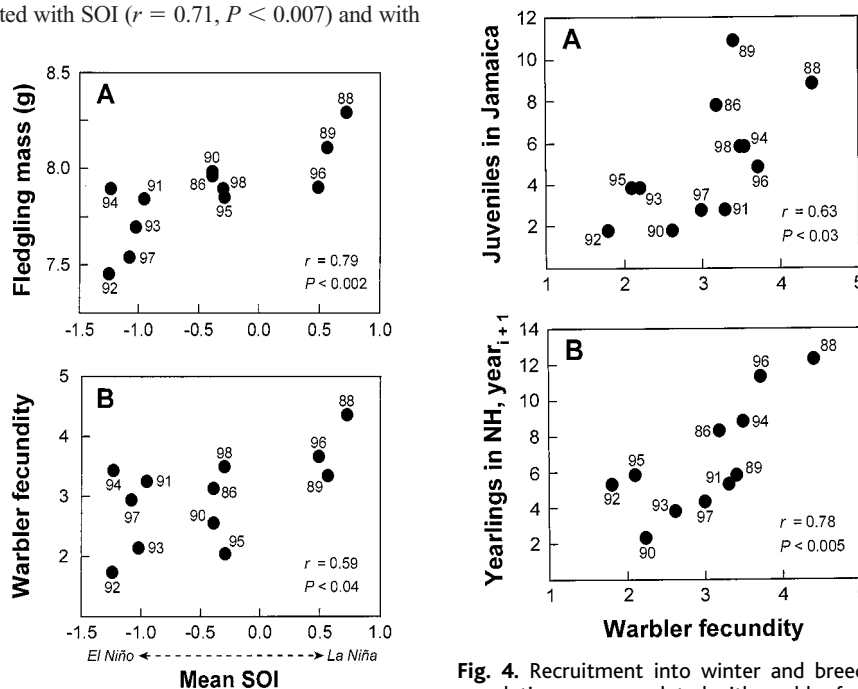


Fig. 3. Reproductive parameters of black-throated blue warblers were correlated with ENSO phase. X axis, mean monthly SOI. Numbers by data points indicate year; data were lacking for 1987. (A) Mean mass of warbler chicks at fledging, a predictor of offspring survival (15). (B) Warbler fecundity, i.e., mean number of offspring fledged per warbler pair per year after controlling for nestling mass (17).

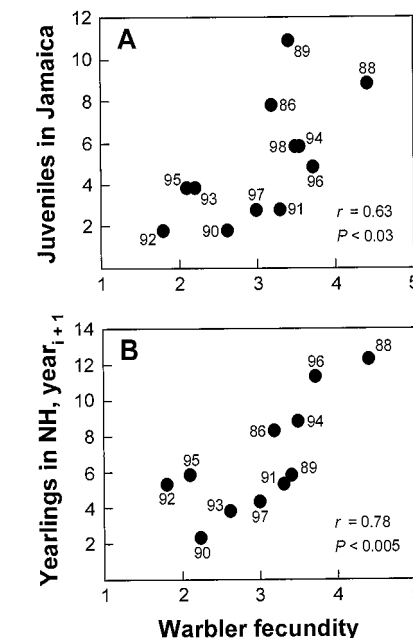


Fig. 4. Recruitment into winter and breeding populations was correlated with warbler fecundity. X axis, mean warbler fecundity in year_i (17). Only males were included in these analyses due to uncertainty in determining the age of female black-throated blue warblers. Numbers by data points indicate year_i; data were lacking for 1987. (A) Number of juvenile males at the Jamaica site each October in year_i. (B) Number of yearling males at the New Hampshire site each May in year_{i+1}.

- ing 8000 understory leaves on transects through the study plot and recording length of each larva present. Larval lengths were converted to biomass using length-mass regressions.
20. No banded fledglings from the 64-ha plot in New Hampshire have returned to the plot as breeding adults, nor have any been resighted on winter quarters. Thus, the relations between annual fecundity and recruitment documented here represent warbler population dynamics occurring at a larger, regional scale.
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 31. We used Cormack-Jolly-Seber models (29) and the MARK computer program (30) to estimate warbler survival and recapture probabilities. Survival from year_i to year_{i+1} was modeled as constant, as dependent on year, and as a linear function of mean monthly SOI in year_i. Recapture probability was modeled as either constant or as dependent on year. We did not model age- or sex-related differences in these parameters because of small sample

sizes from Jamaica. Identical but separate models were run for the Jamaica and New Hampshire populations. Model details can be found at *Science Online* at www.sciencemag.org/features/data/1049756/shl.

32. Funded by grants from the NSF. We are grateful for the advice and assistance of M. Ayres, D. Bolger, K. Cottingham, P. Doran, M. Johnson, W. Lowe, P. Marra, M. McPeck, S. Morrison, L. Nagy, J. Nichols, P. Roberts, K. Sillett, S. C. Sillett, and A. Strong. We thank the Jamaica Natural Resources Conservation Authority, the Williams and Sutton families of Jamaica, and the Hubbard Brook Experimental Forest of the U.S. Department of Agriculture's Northeastern Research Station for their support and cooperation.

23 February 2000; accepted 26 April 2000

Designing Small-Molecule Switches for Protein-Protein Interactions

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Mutations introduced into human growth hormone (hGH) (Thr¹⁷⁵ → Gly-hGH) and the extracellular domain of the hGH receptor (Trp¹⁰⁴ → Gly-hGHbp) created a cavity at the protein-protein interface that resulted in binding affinity being reduced by a factor of 10⁶. A small library of indole analogs was screened for small molecules that bind the cavity created by the mutations and restore binding affinity. The ligand 5-chloro-2-trichloromethylimidazole was found to increase the affinity of the mutant hormone for its receptor more than 1000-fold. Cell proliferation and JAK2 phosphorylation assays showed that the mutant hGH activates growth hormone signaling in the presence of added ligand. This approach may allow other protein-protein and protein-nucleic acid interactions to be switched on or off by the addition or depletion of exogenous small molecules.

A large number of cellular processes involve specific protein-protein or protein-nucleic acid interactions, including signal transduction, transcription, cellular trafficking, and mitosis. Many of these interactions are regulated either by posttranslational modification (e.g., phosphorylation, acylation, and methylation) or by binding of ligands such as guanosine triphosphate, cyclic adenosine monophosphate, and hormones. There are few general strategies for the generation of synthetic molecules that directly modulate these interactions. Here we report a two-step approach for regulating biomolecular interactions. First, a cavity is introduced at a protein-protein or protein-nucleic acid interface that results in a loss of binding energy. A library of small molecules is then screened for ligands that bind the cavity and restore the protein-protein or protein-nucleic acid interface. Using this strategy, we generated a ligand-gated growth factor-growth factor receptor interaction between human growth hor-

hormone (hGH) and its receptor (1, 2).

The initial event in signaling through the hGH receptor is the binding of hGH to site 1 of the extracellular domain of the receptor (hGHbp) to form a high-affinity complex (dissociation constant $K_d = 0.3$ nM). A high-resolution x-ray crystal structure (3) of this complex reveals an interface of about 1300 Å² that involves 31 side chains on the hormone and 33 residues on the receptor (4). Alanine scanning mutagenesis revealed that Trp¹⁰⁴ and Trp¹⁶⁹ of hGHbp are critical binding determinants (4). The binding affinity of the Trp¹⁰⁴ → Ala mutant of hGHbp is reduced by more than 2500-fold relative to wild-type hGHbp. The side chains of these residues pack with surrounding nonpolar side chains from both hGH and hGHbp to form a hydrophobic core that, together with a network of hydrogen bonds and five interprotein salt bridges, makes up the protein-protein interface (5). It has been shown that interface remodeling that repacks the 150 Å³ cavity introduced by the Trp¹⁰⁴ → Ala mutation can restore a substantial fraction of the binding energy (6). Similar results have been found with mutations to the hydrophobic cores of other proteins (7). In addition, a mutant of

T4 lysozyme was stabilized by incorporation of exogenous benzene into a hydrophobic cavity in the protein interior (8). Benzene also shifted the dimer-trimer equilibrium of a GCN4 leucine zipper Asn¹⁶ → Ala mutant by binding to a hydrophobic cavity in the trimer (9).

These results suggested that it might be possible to selectively repack a hydrophobic cavity created at the hGH-hGHbp interface with an exogenous small molecule. Such a molecule might be expected to act as a molecular switch—addition of the ligand should result in binding of a low-affinity hGH mutant to the receptor and activation of the signaling pathway. To test this notion, we substituted Trp¹⁰⁴ in hGHbp and Thr¹⁷⁵ in hGH with glycine. The Thr¹⁷⁵ → Gly mutant was expected to further reduce the interaction between the two proteins (the binding affinity of the Thr¹⁷⁵ → Ala mutant is reduced 25-fold) and make the cavity at the interface larger to accommodate indole analogs that might complement the defect.

To screen for small molecules that complement the hGH-hGHbp interface defect, we panned phage-displayed hGH against immobilized hGHbp in the presence of added ligand. This assay allows one to further optimize cavity shape by screening a phage-displayed hGH library for mutants that improve the ligand-“hole” complementarity. hGH was displayed on the NH₂-terminus of pIII protein of filamentous phage as previously described (10). The Trp¹⁰⁴-hGHbp mutant was immobilized on streptavidin-coated magnetic beads through a unique biotinylated cysteine generated by mutation of surface Ser²⁰¹ (11). This residue is distant from binding site 1 but blocks the second hGH-hGHbp interface (site 2) when linked to a solid support (4). A library of roughly 200 indole derivatives and derivatives of structurally related 5- and 6-membered fused aromatic heterocycles including benzimidazoles, quinolines, isoquinolines, benzothiazoles, and purines was screened for ligands that complement the binding epitope mutations (12).

To carry out the screen, we divided the small molecule library into 17 groups with about 10 compounds per group; the compounds were dissolved in dimethyl sulfoxide (DMSO)

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