Baleen whale cortisol levels reveal a physiological response to 20th century whaling

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One of the most important challenges researchers and managers confront in conservation ecology is predicting a population’s response to sub-lethal stressors. Such predictions have been particularly elusive when assessing responses of large marine mammals to past anthropogenic pressures. Recently developed techniques involving baleen whale earplugs combine age estimates with cortisol measurements to assess spatial and temporal stress/stressor relationships. Here we show a relationship between baseline-corrected cortisol levels and corresponding whaling counts of fin, humpback, and blue whales in the Northern Hemisphere spanning the 20th century. We also model the impact of alternative demographic and environmental factors and determine that increased anomalies of sea surface temperature over a 46-year mean (1970–2016) were positively associated with cortisol levels. While industrial whaling can deplete populations by direct harvest, our data underscore a widespread stress response in baleen whales that is peripheral to whaling activities or associated with other anthropogenic change.

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For over a century, baleen whales have been subjected to a wide range of anthropogenic disturbances, including: increased shipping, fishing, sound, and numerous pollutants\textsuperscript{1–3}. In general, anthropogenic disturbances are known to elicit a stress response in mammals, with increasing evidence of sub-lethal stressors adversely affecting baleen whales\textsuperscript{6–8}. Understanding the response to sub-lethal stressors becomes crucial because baleen whales are considered sentinels of their environment and indicators of anthropogenic perturbations\textsuperscript{9}. Research involving cetaceans has provided initial evidence that baleen whales respond behaviorally and physiologically to stressors at both a temporal and spatial scale, such as ship traffic or noise\textsuperscript{10–14}.

The physiological response to a stressor, defined as the disruption of an organism’s internal environment, or homeostasis, can lead to system-wide health effects from the scale of an individual to the population\textsuperscript{6,7}. Despite the inherent challenges associated with measuring the stress response of marine mammals, there is a consensus that cortisol, a stress hormone produced through activation of the hypothalamic–pituitary–adrenal axis, is a proxy of the stress response in mammals and positively correlates with the severity of the stressor\textsuperscript{15,16}. Significant challenges hamper direct measurements of cortisol in baleen whales, including sampling cost and logistics, correcting for baseline hormone levels, and the varying longitudinal and temporal resolutions of the tissue or matrix sampled. Techniques have been developed to determine cortisol concentrations from an ever-growing suite of matrices including blood, urine, feces, exhalation, fur/hair and blubber, and some matrices, most notably baleen and cerumen (earwax), provide varying degrees of longitudinal and temporal resolution\textsuperscript{17–22}.

Earplugs from baleen whales (Mysticeti) consist of lipid and keratin-based semiannual bands of alternating dark and light laminae (growth layer groups) formed over the life span of the animal\textsuperscript{23,24}. While historically used as an aging proxy in baleen whales, earplugs also retain both endogenous (e.g. hormones) and exogenous (e.g., persistent organic contaminants) chemicals within the cerumen, providing the ability to describe lifetime chemical profiles\textsuperscript{22,25}. This capacity to archive chemicals along a continuum provides an opportunity to standardize and baseline correct each individual whale’s stress response, revealing a complete retrospective examination of the impacts of potential stressors on free-ranging baleen whales.

Here, we reconstruct lifetime stress profiles from individual baleen whales and assess their relationship to 20th century whaling in the Northern Hemisphere. Specifically, we compare percent change in cortisol from a baseline (baseline-corrected cortisol) with total whaling counts from 1900–1999 to assess whaling as a potential stressor. The term whaling is typically associated with the direct harvest of individual whales, but also encompasses additional anthropogenic extrinsic stressors as well as the ecological consequences of population depletion over time, such as decreased mate abundance. This study represents a link between these sub-lethal, indirect elements of whaling to a physiological stress response in baleen whales.

**Results**

A one hundred and forty six year stress profile. We report 146 years (c. 1870–2016; \(n = 1084\) laminae) of cortisol (ng/g), standardized to baseline-corrected cortisol, to produce lifetime stress profiles from 20 mysticete earplugs representing three species: fin (Balaenoptera physalus), humpback (Megaptera novaeangliae), and blue (Balaenoptera musculus) whales (Fig. 1; \(n = 12, 4, \text{and } 4\), respectively) from the Northern Hemisphere. Eight earplugs sampled from whales originating in the Pacific Ocean had an estimated overall mean age of 31.4 ± 24.2 years ± standard error (± SE) (\(n = 5\) males, mean age 16.8 ± 16.5 years; \(n = 3\) females, mean age 55.8 ± 9.2 years), whereas twelve earplugs from Atlantic Ocean stocks had an overall estimated mean age of 24.9 ± 14.1 years (\(n = 6\) males, mean age 19.9 ± 10.3 years; \(n = 6\) females, mean age 28.9 ± 17.0 years). Cortisol concentrations (ng/g) were determined for each extracted lamina (growth layer representing 6 months), and lifetime profiles were subsequently baseline-corrected for comparison between individuals and among species (Fig. 2). When comparing cortisol levels among species and between sexes, mean baseline-corrected cortisol was significantly highest in fin whales (fin > humpback > blue) (pairwise comparison with Tukey’s method to account for multiple comparisons; \(t = 5.83; \text{P value } < 0.001\)), whereas by sex, male humpback whales had the highest cortisol when compared to blue and fin whales (humpback > blue > fin; mixed-effects linear regression followed by pairwise comparison with Tukey’s method to account for multiple comparisons; \(t = 6.49; \text{P value } < 0.001\); Table 1). There was, however, a significant interaction between sex and age when assessed together in the final regression model (P value < 0.05).

**Whaling numbers and cortisol.** The association between total whaling counts during the 20th century\textsuperscript{26} and baseline-corrected cortisol concentrations (Fig. 3a) was evaluated collectively for all three whale species (years 1900–1999; \(n = 942\) laminae; Fig. 3b; \(r^2 \text{value } = 0.78\); Table 2). Commercial whaling increased in scope and became increasingly more efficient during the 20th century, resulting in a 45% increase in fin whale harvests and a 70% increase in humpback harvests when compared to the 19th century\textsuperscript{26}. This efficacy was maintained during the decade of the 1930s, where ~50,000 fin, humpback, and blue whales were harvested from Northern Hemisphere waters\textsuperscript{26}. During this period, between world wars, maximum baseline-corrected cortisol levels were achieved (53% above baseline) in earplugs, mirroring maximum harvest take of whales (Fig. 3c).

Interestingly, the years 1939–1945 (World War II; WWII) revealed a departure from the close association between mean cortisol concentrations and mean whaling harvests (\(n = 10\) earplugs, \(n = 225\) laminae; Fig. 3a, b). Specifically, during the WWII era, baseline-corrected cortisol
within earplug laminae increased 10% while whaling harvests decreased to the lowest numbers observed during the pre-whaling moratorium era (pre-1986) in the Northern Hemisphere (Fig. 3a).

While it remains unknown if a 10% increase in baseline-corrected cortisol represents an adverse physiological or behavioral response, the departure from the close association with whaling counts may be in response to other stressors such as marine-based wartime activities. In other words, the stressors associated with activities specific to WWII may supplant the stressors associated with industrial whaling for baleen whales. Therefore, we surmise that wartime activities (e.g., underwater detonation of ordinance, naval battles including ships, planes, and submarines), as well as increased vessel numbers, contributed to increased baseline-corrected cortisol concentrations during this period of reduced whaling. With the extensive migration patterns of baleen whales, interaction with widespread wartime activities would seem plausible and deleterious to baleen whales.

Once post-war whaling resumed in the 1950s, the number of whales harvested drastically increased and peaked in the early 1960s, with nearly 150,000 animals harvested. During the early

| Whale species and sex (n) | Percent from baseline mean/median (SD) |
|-------------------------|----------------------------------------|
| Fin whale               | 63.48/57.34 (39.58)                    |
| Male (8)                | 52.78/43.72 (39.86)                    |
| Female (4)              | 77.66/78.21 (34.5)                     |
| Humpback whale          | 43.73/38/35 (31.17)                    |
| Male (1)                | 96.30/84/76 (49.44)                    |
| Female (3)              | 37.57/34.42 (21.14)                    |
| Blue whale              | 48.53/37.00 (37.71)                    |
| Male (2)                | 77.02/86.45 (39.14)                    |
| Female (2)              | 30.66/25.18 (23.11)                    |

Table 1 Baseline-corrected cortisol, mean/median, and standard deviation (± SD) for large whale earplugs (N = 20)
1960s, baseline-corrected cortisol peaked to a maximum 68%, denoting the highest mean baseline-corrected stress values over the 20th century (Fig. 3a). Comparing 5-year mean groupings in baseline-corrected cortisol, the lowest 5-year means spanned the years 1970–1999, whereas the highest 5-year means occurred during the 1920s, 1950s, and 1960s (Fig. 3b). A decline in both whaling numbers (7.5% yr\(^{-1}\)) and a corresponding decrease in cortisol levels (6.4% yr\(^{-1}\)) occurred during the mid-1970s, when protective whaling moratoriums were adopted in the United States (Marine Mammal Protection Act of 1972 = red line, Fig. 3a). Whaling harvest counts decreased 75% for fin, humpback, and blue whales in the Northern Hemisphere during this period\(^{26}\). This period of dwindling harvest counts coincided with the lowest baseline-corrected cortisol concentrations measured from whale earplugs over the 20th century (27% above the baseline value; Fig. 3a, b). We propose that this close association between baseline-corrected cortisol concentrations and whaling harvests indicates a relatively prompt response by baleen whales to the direct and indirect activities of whaling. From the 1970s through the 2010s (\(n = 132\) laminae; \(n = 6\) earplugs), as whaling counts were reportedly zero in the Northern Hemisphere, mean baseline-corrected cortisol
levels steadily increased (Fig. 3b), with recent peaks reaching near the maximum levels observed before the whaling moratorium (Fig. 3b).

Recent anthropogenic stressors. Recent modeling efforts estimate the impact of several anthropogenic drivers toward ecological change with sea-surface temperature (SST) anomalies (1985–2005) as the most pronounced stressor in marine ecosystems. According to the Intergovernmental Panel on Climate Change, the ocean has warmed on a global scale, by an average of 0.11 °C per decade from 1971 to 2010. To assess the increases in stress in baleen whales and to evaluate specific anthropogenic stressors, an anthropogenic pressure index specifically for baleen whales (APIw) was generated (Supplementary Table 1, Supplementary Table 2). Although the variables sex and age did not independently explain the observed deviations in baseline-corrected cortisol (Model E—Supplementary Table 3), their importance in the final model indicates these two variables do account for some of the variation in cortisol levels not accounted for by whaling harvest counts. The significant negative coefficient for the interaction variable (sex/age) indicates that, overall, females in this study experienced less stress than did males over their lifetime. Specifically, mean baseline-corrected cortisol was ~12% less for females over a lifetime. In other words, adult males had significantly elevated baseline-corrected cortisol levels (P value = 0.004; linear mixed-effects model, Table 2; Supplementary Figure 1).

In univariate regression analysis, the relationship between yearly whale harvest counts and baseline-corrected cortisol was independently significant (P value = 0.001). After including yearly whale counts in the final multivariate model, this positive relationship continued to be significant, with baseline-corrected cortisol increasing as the number of harvested whales increased (Fig. 3b, Table 2). For example, when yearly harvested whales numbered in the mid-range of 7000–9999 (corresponding to the decades: 1900s, 1930s–1940s), the baseline-corrected cortisol was higher compared to yearly harvest counts numbering <7000 (corresponding to the mid-1970s–2010s) and less than those yearly totals corresponding to higher harvest levels (>10,000 during the 1910s, 1950s, and 1960s).

We show a positive relationship between activities associated with commercial whaling harvests and baseline-corrected cortisol from baleen whale earplugs spanning the 20th century (Fig. 3b). While industrial whaling is known to deplete populations by direct harvest, our data underscores that stress was not only a result of direct harvest on targeted individual whales, but also increased in whales not directly harvested. Although unable to account for the individual components of whaling effort through time such as changes in whaling methodologies and number of ships, our results illustrate a critical link between whaling and stress in baleen whales. Combining multiple life history profiles characterized the effect of whaling on baseline-corrected cortisol in baleen whale populations; however, it should be noted that datasets from individual whales exhibit the variability of a complex life history (Table 3, Fig. 2). Taken individually, these life history profiles cannot easily capture temporal patterns or anthropogenic events.

Table 2 Results of fitting a linear mixed-effects model to determine the level of baseline-corrected cortisol in earplug of large baleen whales (1900–1999) given sex, age, sex/age interaction, and number harvested over 5-year intervals

| Variable | Coefficient | SE | Wald z | P-value |
|----------|-------------|----|--------|---------|
| Percent cortisol above baseline | Sex (female versus male) | -0.461 | 12.700 | -0.04 | 0.971 |
| Age category (years) | 11–24.9 | 9.789 | 3.288 | 2.98 | 0.003 |
| ≥ 25 | 19.054 | 5.949 | 3.20 | 0.001 |
| Sex/age category interaction | -9.880 | 3.4424 | 2.89 | 0.004 |
| Number of whales harvested each year | 0.005 | 0.002 | 3.18 | 0.001 |

SE, standard error

Age = <11, 11–24.9, ≥ 25 years. The reference values were sex = male, age category = <11 years.

Significant predictors are those with P values ≤ 0.05.
overall trends in baseline-corrected cortisol from earplugs in this study did not moderate with time (Fig. 3a), possibly indicating a conserving of the stress response. In other words, these whales closely mirrored the stress of their surroundings. This reinforces the concept of large baleen whales as sentinels of the marine environment. Additionally, the intercept of the association between the 5-year mean whaling counts and baseline-corrected cortisol is ~20%, which may represent the basal level of cortisol in the absence of whaling.

The influence of increased SST anomalies on baseline-corrected cortisol in the present study is insignificant prior to the 1970s ($r^2$ value = 0.01). However, from the 1970s to 2016, increased SST anomalies were positively associated with baseline-corrected cortisol (Fig. 3c; $r^2$ value = 0.46). Currently, changes in SST anomalies appear to be one of the dominant drivers of cumulative anthropogenic impacts on marine ecosystems, though other anthropogenic stressors, such as increased sound, pollutants, over-fishing, and ocean acidification likely contribute to increased cortisol in baleen whales. As more earplugs from current whale mortalities are collected, the association between anthropogenic drivers and their effects on large baleen whales can be refined.

One of the most important challenges researchers and managers confront in conservation-based ecology is predicting how populations will respond to sub-lethal natural, environmental, and anthropogenic stressors, as well as the cumulative effect of these stressors. This study illustrates the importance of using matrices such as earplugs to reconstruct lifetime profiles, determine baseline hormone values, and model retrospective data to determine potential associations with past or present anthropogenic stressors. While this study focused on the stress hormone cortisol in baleen whales and its relationship to potential anthropogenic stressors through time, measuring additional hormones or analytes offers an opportunity to examine the impacts of chronic stress on whale behavior including migration patterns through stable isotope analysis and fecundity through progesterone measurements.

Long-lived organisms endure evolutionary pressures resulting from a rapidly changing environment to which whales must quickly adapt. Given the current pace of change over the past century, this capacity, or plasticity, to respond promptly may be compromised. Current anthropogenic stressors may have a greater deleterious effect to species already compromised by the significant population declines associated with a 100+ years of industrial whaling. While we established an association between industrial whaling and stress in baleen whales over the 20th century, additional anthropogenic factors, such as recent SST anomalies due to climate change, increased fishing and krill harvests, and sea ice decline should be considered and further studied during 21st century post-whaling in the Northern Hemisphere.

**Methods**

**Earplug acquisition.** A total of 1084 earplug lamina from three species, spanning 146 years, yielded a subset of laminae ($n = 942$) corresponding with published 20th century whaling counts (1900–1999). Baleen whale earplug samples were originally collected during whaling activities during the 20th century (pre-1972) and subsequently archived in museums (Smithsonian Museum of Natural History or National History Museum of London) or extracted from recent stranded carcasses (Table 3).

**Aging.** Baleen whale earplugs were weighed and measured before storing in a −30 °C until processing. After removal from the freezer, all earplugs were bisected using medical grade zirconia ceramic scalpel blades or ceramic knives. A frozen bisected earplug was polished using progressively finer grit, rinsed using deionized water and photographed using a Canon DSLR camera with macro lens (Canon 6D Mark II). The SLR camera was mounted to a copy stand with adjustable fluorescent lighting (Benchlight Copymate). Digital photographs were taken and used to age the whale by counting the number of dark and light laminae, assuming the combination of one dark and one light lamina (growth layers) constitutes one year of life. Before delamination, two independent readers used digital photographs to age each earplug included in this study. One additional reader was used if there was greater than a ± 5% discrepancy in the total laminae counts.

**Sectioning whale earplugs.** Baleen whale earplugs ($n = 20$; Table 3) were meticulously delaminated ($n = 1084$ using a ceramic scalpel under magnification (head-mounted magnifier loupes (10–20x))). Each separated lamina was weighed to the nearest 0.001 g, placed into a glass vial, filled with nitrogen and stored at −30 °C until processed.

**Stress-related hormone radioimmunoassay technique.** Cortisol concentrations were determined in each lamina using an enzyme-linked immunosorbent assay

### Table 3 Mean cortisol as a percent change from baseline (baseline-corrected) and standard error (± SE) for fin, humpback, and blue whales in the N. Hemisphere as related to location (ocean basin), sex, estimated age (years), and life span

| Species | Location | Sex | Age estimates (years) | Lifespan | Mean %BL cortisol ± SE | %BL cortisol range | %BL cortisol $r^2$ slope |
|---------|----------|-----|----------------------|----------|-----------------------|-------------------|------------------------|
| Fin     | Pacific  | M   | 35                   | 1929.5-1964 | 99.9 ± 7.5             | 2.6-187.7          | 0.67                   |
|         | Pacific  | M   | 33.5                 | 1928.5-1961.5 | 43.3 ± 5.6             | 9.7-198.7          | 0.20                   |
| Atlantic| M        | 22.5| 1933-1955            | 39.9 ± 2.4     | 1.2-67.9               | 1.3               |
| Atlantic| M        | 38.5| 1871.5-1909.5        | 48.2 ± 2.5     | 7.8-103.7             | 0.08               |
| Atlantic| F        | 13  | 1943.5-1956          | 29.1 ± 3.6     | 7.4-78.2               | 0.02               |
| Atlantic| F        | 19  | 1936.5-1955          | 68.8 ± 4.3     | 1.6-116.4             | 0.00               |
| Atlantic| F        | 53  | 1902.5-1955          | 78.7 ± 2.5     | 6.0-129.1             | 0.02               |
| Atlantic| F        | 48  | 1915.5-1963          | 69.4 ± 3.2     | 11.5-126             | 0.20               |
| Atlantic| M        | 11.5| 1918.5-1929.5        | 38.4 ± 6.8     | 8.9-143.9            | 0.12               |
| Pacific | M        | 2   | 2013-2015            | 3.3 ± 2.3      | 1.4-10.1             | 0.40               |
| Pacific | M        | 1.5 | 2013.5-2015          | 8.2 ± 7.9      | 2.6-24.0              | 0.95               |
| Atlantic| M        | 18.5| 1948.5-1964.5        | 25.2 ± 2.0     | 2.4-60.1             | 0.08               |
| Humpback| Pacific  | F   | 45.5                 | 1954.5-1999.5  | 26.7 ± 1.7             | 1.3-47.9          | 0.16                   |
|         | Pacific  | F   | 59                   | 1955-2014     | 28.6 ± 1.6            | 1.9-58.2          | 0.08                   |
|         | Pacific  | F   | 63                   | 1940-2003     | 41.8 ± 1.2             | 14.5-69.2         | 0.16                   |
| Blue    | Atlantic | M   | 16.5                 | 1948.5-1964.5 | 89.5 ± 10.2            | 2.5-187.9         | 0.08                   |
|         | Atlantic | F   | 19.5                 | 1935.5-1954.5 | 24.8 ± 2.7             | 1.4-60.3          | 0.00                   |
|         | Atlantic | F   | 21                   | 1934.5-1955  | 42.6 ± 4.8              | 3.3-110.8        | 0.19                   |
|         | Atlantic | M   | 11.5                 | 1937-1948     | 55.8 ± 8.0            | 8.7-111.5       | 0.01                   |
|         | Pacific  | M   | 12                   | 1995-2007     | 63.9 ± 7.1            | 43.9-156         | 0.13                   |

*%BL cortisol $r^2$ slope denotes cortisol linear regression value over lifetime of whale. *denotes recent earplugs.*
with the exception of SST anomalies, these additional anthropogenic variables were incorporated into the models using harvest counts obtained from the National Oceanic and Atmospheric Administration (NOAA) and were categorized into seven deviation levels ranging from −0.90 to 0.50 with approximate corresponding years for each category. Univariate models were developed to assess the individual relationship between each predator variable and the response variable (baseline-corrected cortisol). Those predictor variables associated with baseline-corrected cortisol at a P value of ≤0.25 in univariate analysis were included in the initial full model, as well as those variables of biological interest or identified in the literature as potential covariates. Each of the covariates was individually removed from the full and reduced models as needed to form the most parsimonious model based on likelihood ratio tests and Akaike Information Criterion (Akaike 1973). If the removal of a variable caused another variable’s coefficients to change more than 10%, then the latter variable was retained, indicating the model was sensitive to its inclusion. Estimation of partitioning factors was by restricted maximum likelihood using the Stata “xtmixed” command for mixed-effects models (Stata Corp., College Station, Texas 77845, USA).

Mean baseline hormone concentration was determined by averaging the lowest three cortisol concentrations within each individual earplug. Using this average value, percent change from mean baseline value (absolute value, baseline-corrected) was calculated for each subsequent time point within each earplug over the entire whale life span by the formula

$$
\%BL = \left(1 - \frac{C_i - C_{BL}}{(C_0 + C_{BL})/2}\right) \times 100
$$

with $C_i$ cortisol concentration (ng/g) and $C_{BL}$ the mean baseline value for the individual earplug. To evaluate potential uncertainty in baseline values, a sensitivity analysis was conducted by calculating mean values for additional concentration pools using the lowest three and lowest five cortisol concentrations from five individual whales from three species. The sensitivity analysis revealed that the lifetime regression trend was identical among the three groupings (lowest, mean lowest 3, and mean lowest 5), however, using the mean lowest three concentrations as a means to baseline values resulted in lower mean error from percent change from baseline modeling (see above) was used to assess the relationships of species, age, and time (based on age/lamina counts and collection dates) with baseline-corrected cortisol among all earplugs sampled. 20th century whaling data was obtained from Rocha et al., and used to fit with mean 5-year cortisol baseline data over the same period (least linear squares). The standard error of the mean (±SE) was calculated where $\sigma$ is the standard deviation (±SD) of the population and $n$ is the number of earplugs.

### Data availability
All relevant data are available from the authors upon reasonable request.

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Author contributions

S.J.T. and S.U. developed this discipline, conceived the idea for this study, and wrote the manuscript. S.A.N. performed modeling/statistical analyses and contributed(edited drafts of the manuscript. D.C. and F.M. delaminated/aged earplugs and completed hormone assays. Z.W. assisted in hormone assays. C.W.P. and R.S. provided archived earplugs as well as insight. C.G. provided contemporary earplug samples.

Additional information

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