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BASELINE NORMAL VALUES AND PHYLOGENETIC CLASS OF THE ELECTROCARDIOGRAM OF ANESTHETIZED FREE-RANGING BROWN BEARS (*URSUS ARCTOS*)

A. Rae Gandolf,[1,8] Åsa Fahlman,[2,3] Jon M. Arnemo,[4,5] James L. Dooley,[6] and Robert Hamlin[7]

[1] 2615 E Newman St., Zanesville, Ohio, USA
[2] Department of Pathology and Wildlife Diseases, National Veterinary Institute, SE-751 89 Uppsala, Sweden
[3] Section of Anesthesiology, Department of Clinical Sciences, Faculty of Veterinary Medicine and Animal Science, Swedish University of Agricultural Sciences, PO Box 7054, SE-750 07 Uppsala, Sweden
[4] Faculty of Forestry and Wildlife Management, Hedmark University College, Campus Evenstad, NO-2418 Elverum, Norway
[5] Department of Wildlife, Fish and Environmental Studies, Faculty of Forest Sciences, Swedish University of Agricultural Sciences, SE-901 83 Umeå, Sweden
[6] Muskingum College, Science Division, 163 Stormont St., New Concord, Ohio 43762, USA
[7] Ohio State University College of Veterinary Medicine, 1900 Coffey Rd., Columbus, Ohio 43210, USA
[8] Corresponding author (email: raegandolf@yahoo.com)

ABSTRACT: Electrocardiographic (ECG) variables were measured in 22 healthy, free-ranging brown bears (*Ursus arctos*) anesthetized with a combination of medetomidine, tiletamine, and zolazepam during research and management operations in south-central Sweden. Six-limb lead ECGs and the base-apex lead were recorded. Morphologies, amplitudes, rhythms, and durations of P waves, PQ intervals, QRS complexes, T waves, QT intervals, and QT intervals corrected for heart rate (QTc) were calculated from the base-apex lead. The mean electrical axis (MEA) for each individual was approximated in the frontal plane from the heights of R waves in leads I (X axis) and aVF (Y axis). All 22 bears had sinus rhythms and 10 of them had respiratory sinus arrhythmia. Heart rates ranged from 43 to 103 beats per minute and were independent of body mass. The MEA was 78.6 (±5.5) degrees. Some bears had strikingly peaked T waves, and many had pronounced notching (high frequency components) to the QRS complex. This information contributes to the limited data base of electrocardiography for brown bears and elucidates ECG similarities with other species in the order Carnivora.

Key words: Bear, ECG, electrocardiogram, heart, T wave, *Ursus arctos*.

INTRODUCTION

Brown bears (*Ursus arctos*) range throughout the northern hemisphere and are listed as threatened by the IUCN. The largest populations are found in northern regions of North America and Eurasia, with more fragmented populations in western and southern Europe and small remnant populations in areas of the Middle East and Central Asia. Sweden's brown bear population recovered from near extinction in the 1930s to a current population of approximately 3,300 (Kindberg et al., 2009). The successful repopulation is attributed to policy and active management, supported by health and ecological research by the Scandinavian Brown Bear Research Project that was established in 1984. Up to 100 bears are immobilized annually through this project.

Electrocardiography (ECG) is the best noninvasive method to evaluate cardiac electrophysiology in anesthetized wildlife and is therefore valuable in both patient monitoring during anesthesia and for evaluation of cardiac health. Portable, battery-powered, multifunction ECG units also can be used for monitoring pulse oximetry, end tidal CO_2, blood pressure, heart rate, and respiratory rate. Some aspects of cardiac physiology have been studied in bears, primarily in an attempt to extrapolate information to heart conditions in humans, such as sudden infant death syndrome and hibernating myocardium, and to further understand the physiology of hibernation (Folk et al., 1974; Nelson et al., 2003). However, there are few measurements available for interpreting normal ECG variables in brown bears. Although heart disease does not appear to be a substantial health issue for ursids, diseases reported in bears include

bacterial endocarditis in a black bear (*U. americanus*; McBurney et al., 2000), Chagas' cardiopathy in a polar bear (*U. maritimus*; Jaime-Andrade et al., 1997), and tetralogy of Fallot in a brown bear (Ågren et al., 2005).

The goal of this study was to provide baseline data for electrocardiography in anesthetized free-ranging brown bears. Specifically, evaluations were planned using tiletamine–zolazepam–medetomidine anesthesia since it is the currently preferred chemical immobilization combination for this species (Fahlman, 2008) and would therefore provide the most widely usable information.

MATERIALS AND METHODS

This study was conducted in April 2006 (springtime) in south-central Sweden (61°N, 13°E), on 22 free-ranging brown bears (20 females and two males) ranging from 1 to 19 years of age and from 15 to 224 kg. Age was determined based on an established family tree derived from in-depth population monitoring that has occurred in the region since 1984. Ambient temperatures during the capture events ranged between 2.5 C and 19.7 C, with approximately 13 hr of daylight. The bears were immobilized for individual marking for ecologic, genetic, and health studies by the Scandinavian Brown Bear Research Project.

Each bear was chemically immobilized using a combination of medetomidine HCl (Domitor®, 1 mg/ml, or Zalopine®, 10 mg/ml, 0.03–0.08 mg/kg, intramuscularly [im]; Orion Pharma Animal Health, Turku, Finland), and lyophilized tiletamine–zolazepam (Zoletil®, 500 mg/vial, 1.2–4.2 mg/kg, im; Virbac, Carros, France) administered by darting from a helicopter, according to an established protocol (Arnemo and Fahlman, 2008). Following anesthetic induction, a complete physical examination was performed on each animal. No bears had indications of illness or injury. One facet of a concurrent study included venous blood collection for determination of serum electrolytes for 14 of the bears. Electrocardiograms were obtained using a portable, multifunction monitor with electrocardiograph (Propaq® Encore, Welch Allyn, Beaverton, Oregon, USA) including frequency response, filter, and electrodes. To minimize variables associated with anesthetic depth, recordings were made once a surgical anesthesia plane was attained, based on lack of response to stimuli and lack of jaw tone. Recordings were made with bears in right lateral recumbency with thoracic limbs at near right angle to the long axis of the torso. Two methods of electrode attachment were evaluated on the initial 10 bears to determine which type of lead attachment resulted in tracings with the least artifact and sharpest deflections. In the first method, alligator clips were clamped onto the skin over the olecranons and patellas and isopropyl alcohol was used as a solubilizing medium at those sites. For the second method, adhesive leads were placed onto the front and rear central foot pads and secured with elastic bandage material. The limb lead ECGs (I, II, III, aVR, aVL, aVF) were recorded at a paper speed of 25 mm/sec. Configurations, durations, and amplitudes of P waves, QRS complexes, and ST-T complexes were analyzed for all leads. Cardiac rhythm, heart rate, and durations and/or amplitudes of P, PQ, QRS, T, QT, R and R-R segments were measured from lead II (Fig. 1). QT was corrected (QTc) for heart rate using the equation: $QTc = QT/\sqrt{\text{R-R interval}}$. The mean electrical axis (MEA) of QRS was approximated from amplitudes of R waves in leads I (X axis) and aVF (Y axis). Because the QRS complex in lead aVF of bears is predominantly an R wave, the Q and S waves were neglected and were not subtracted from the heights of the R waves. The QRS complex in lead I was usually of low amplitude and contained negative and positive deflections of nearly equal amplitudes; therefore, the sum of all components of QRS was taken as the amplitude of the deflection in lead I. Because ventricular repolarization began immediately after the end of QRS and there was no ST segment, as in most mammals (Hamlin and Smith, 1965), the complex representing ventricular repolarization is termed the ST-T. The orientation of the ST-T in the frontal plane was estimated in a similar fashion to that for QRS; however, the ST-Ts were always positive when the QRS complexes were predominantly positive. The standard frontal plane reference system was used, in which the subject is viewed from the ventral aspect so that 0° is to the left and 90° to the tail. Sinus rhythm was identified by positive P waves in leads I and aVF, and the fact that every P was followed by a QRS and every QRS was preceded by a P with a reasonably fixed PQ interval. A sinus arrhythmia was identified when succeeding P-P intervals varied by >15%. Only leads I and aVF were analyzed, because they define the frontal plane (I the X-axis and aVF the Y-axis), and using the biaxial reference system allows synthesis of ECGs in all other frontal plane leads.

Statistical analyses were performed using the statistical software package SPSS 9.0

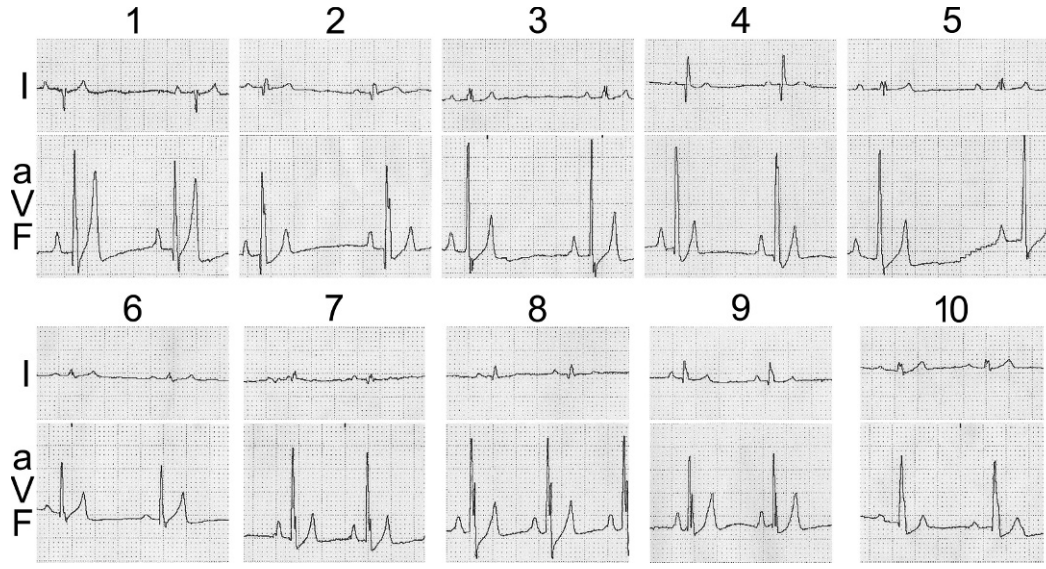

FIGURE 1. Examples of electrocardiogram recordings of 10 anesthetized, free-ranging brown bears, in leads I and AVF, captured in April 2006 in Sweden.

(SPSS, Inc., Chicago, Illinois, USA) to evaluate durations of P, PQ, and QRS. Relationships were sought between component deflections and both body weight and heart rate using linear regression analysis. Bears were separated into three groups (1 yr, 2–3 yr, and >3 yr) because of the limited sample sizes for each specific age. Differences in heart rate according to age were evaluated using Analysis of Variance (ANOVA). Differences associated with sex were not evaluated, given the overly disproportionate sampling (20 females and two males). Relationships were deemed statistically significant when $P<0.05$.

RESULTS

Electrocardiograms of good quality for interpretation were obtained from all 22 bears. Examples of lead I and aVF ECGs from 10 bears are shown (Fig. 1). The adhesive method of applying electrodes resulted in component deflections of slightly lower amplitudes containing fewer extraneous notches, but ECGs obtained by both methods were adequate for interpretation (Fig. 2).

All bears maintained sinus rhythms, and 10 (45%) had subtle respiratory sinus arrhythmias. Values for variables including amplitudes and durations of component deflections are shown in Table 1. Regression plots of component deflections are shown versus body weight (Fig. 3) and versus heart rate (Fig. 4). The only statistically significant relationship among the variables versus heart rate or body weight was between PQ interval and body weight ($Y=0.325x+146.6$, $P<0.05$, $r^2=0.24$). No statistical significance was found when comparing age group or body weight to heart rate (Fig. 5). Orientation of mean P and QRS vectors in the frontal (ventral) plane are quite similar to each other and to orientations of the same ECG components in man and dog (Hamlin and Smith, 1965),

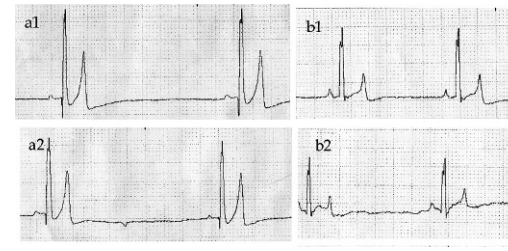

FIGURE 2. Comparisons of electrocardiograms recorded using alligator clips (a1 and b1) versus sticky pads (a2 and b2) in two anesthetized brown bears captured in April 2006 in Sweden.

TABLE 1. Mean±standard deviation (SD) values for electrocardiogram and physiologic variables in 22 anesthetized free-ranging brown bears captured in April 2006 in Sweden.

Variable	Mean±SD
Body weight (kg)	57.9±48.3
Age (yr)	4.6±5.5
Heart rate (beats/min)	71±15
P duration (msec)	78±13
PQ interval (msec)	165±32
QRS duration (msec)	55±12
QT interval (msec)	253±25
QTc interval (msec)	273±22
P amplitude (mV)	0.29±0.13
T amplitude (mV)	0.72±0.35
QRS electrical axis (degrees)	78.6±5.5

and are directed principally caudad and slightly sinistrad. QRS complexes from some bears had easily observed notches and several ECGs demonstrated peaking T waves (Fig. 1).

DISCUSSION

This study provides baseline ECG data for brown bears anesthetized with the currently preferred combination of medetomidine, tiletamine, and zolazepam, in early spring. These or related anesthetic agents are known to alter autonomic cardiac control, albeit less than gaseous agents or many other agents commonly used in veterinary medicine (Hamlin et al., 1966). Sinus arrhythmia is an occurrence that is normal in some species but may also be elicited by anesthesia. Sinus arrhythmia results from irradiations of the medullary ventilatory centers to the juxtaposed cardioregulatory centers, which decrease vagal efferent activity

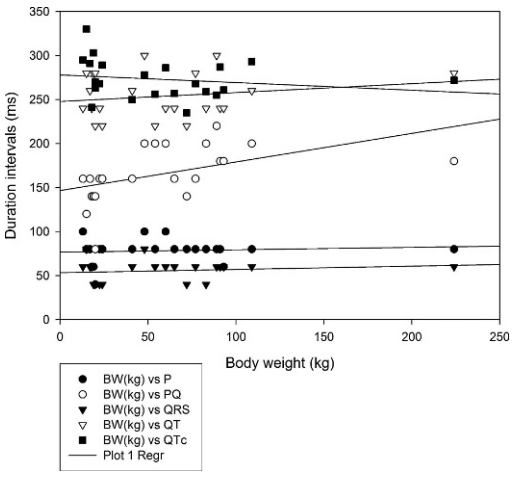

FIGURE 3. Plots of electrocardiogram component deflections versus body weight in anesthetized brown bears captured in April 2006 in Sweden. Only the plot of body weight versus PQ interval demonstrates a statistically significant relationship ($P<0.05$, $r^2=0.2379$).

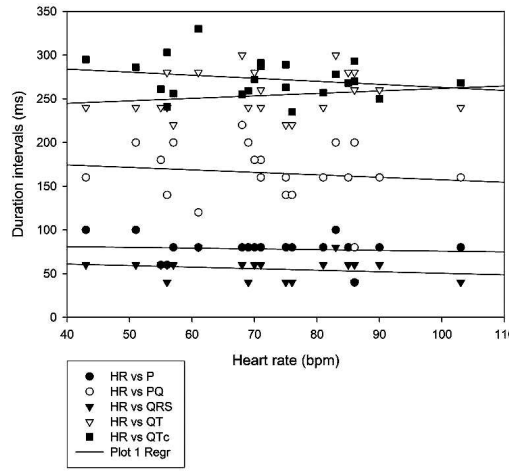

FIGURE 4. Plots of electrocardiogram component deflections are shown versus heart rate in anesthetized brown bears captured in April 2006 in Sweden. None of the relationships were statistically significant ($P>0.05$).

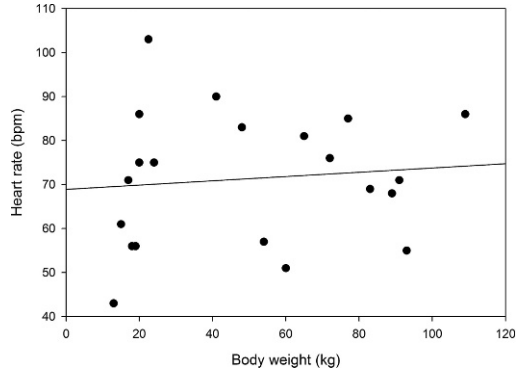

FIGURE 5. Plot of body weight versus heart rate in anesthetized free-ranging brown bears captured in April 2006 in Sweden. This relationship was not statistically significant ($P>0.05$).

(increase in heart rate) during inspiration and increase vagal activity (decrease in heart rate) during expiration. Anesthetics may either suppress rate of sinoatrial nodal discharge, which slows heart rate, or may possess parasympatholytic or sympathomimetic properties that speed rate of discharge of sinoatrial node and diminish respiratory sinus arrhythmia (Linker and Camm, 1988). The finding of mild sinus arrhythmia in fewer than half the bears in this study likely reflects these parasympatholytic or sympathomimetic properties of the anesthetic agents; sinus arrhythmia would therefore be expected in normal nonanesthetized bears.

The mean heart rate for brown bears in this study of 71 beats per minute (bpm) was between those rates reported for mature grizzly bears (*U. arctos horribilis*) during summer sleep and summer activity (46 and 90 bpm, respectively; Folk et al., 2008) and also between those reported for subadult grizzly bears during activity and hibernation (102 and 54 bpm, respectively; Nelson et al., 2003). This finding may reflect the bradycardic effects of medetomidine (an α_2-agonist), which is typically associated with longer P and QT intervals (Kramer et al., 1992). Although the combination of tiletamine and zolazepam is known to increase heart rate in several species such as polar bears, an increase is not seen when the drugs are combined with medetomidine (Caulkett et al., 1999). Heart rate may vary over the duration of anesthesia, and recordings were not made at consistent time points relative to anesthetic onset in this study. Although there was no significant difference in heart rate of young bears as compared to mature bears in this study, higher heart rates in yearling cubs versus adults were reported in a study with a larger number of subjects anesthetized with the same combination of drugs (Fahlman, 2008).

Electrocardiographic components obtained with alligator clips were generally higher than when obtained with pads (Fig. 2). Although alcohol is widely used as a conducting agent for recording ECGs, it may cause artifact by reducing electrode–skin impedance. Commercially available electrode paste is therefore preferred. Although the pad method was slightly more cumbersome and time consuming, it provided slightly clearer ECG readings and did not require a conducting agent.

Orientations of P and QRS vectors in the frontal plane for brown bears were consistent with depolarization of the atria from the cranially positioned right atrium to the caudally positioned left atrium (P wave) and of the dominant left ventricle with endocardial to epicardial activation (QRS wave). Similar to humans, but different from most other mammals, the orientation of the ST-T vector in the frontal plane is concordant with the orientation of the QRS vector (Hamlin and Smith, 1965). This is indicated by positive T waves in leads aVF and I and is consistent with ventricular repolarization beginning in the subepicardium and ending in the subendocardium.

All mammals fall into two general categories based upon spatial orientation of the QRS vector. Animals of category I are most often primates or carnivores and they have QRS complexes oriented predominantly caudad and ventrad, but slightly sinistrad (Hamlin and Smith, 1965). In lead V10, taken from the dorsal spinous process of the seventh thoracic vertebra, the QRS complex in category I animals is predominantly positive and has a Qr configuration, defined by a large negative initial deflection followed by a small positive terminal deflection (Hamlin et al., 1974). In contrast, the QRS of animals in category II, which comprise the vast majority of the mammalian population including ruminants, ungulates, Equidae, and Suidae, is comprised of an initial small negative deflection followed by a large positive deflection. Although lead V10 was not obtained in the bears of this study, the QRS complexes in leads I and aVF are nearly identical in configuration to those of dogs (*Canis lupus familiaris*), cats (*Felis*

catus), raccoons (*Procyon lotor*), and nonhuman primates (Hamlin et al., 1974), and therefore bears are in category I. This ECG classification is consistent with the phylogenetic classification of Ursidae within the suborder Caniformia, in the order Carnivora, along with the canid, procyonid, mustelid families and all pinnepeds. Furthermore, the relatively short QT intervals (253±25 msec) are similar to those reported for grizzly bears during nonhibernation summer sleep (226±57 msec), and therefore to other classic hibernating species, as concluded by Folk et al. (2008).

The notches observed on the QRS complexes of many of the bears may arise either from fracturing of waves of depolarization as they traverse ventricular myocardium or from minor changes in dominance of the waves of depolarization which shift the orientation of the forces generating the QRS (Flowers and Horan, 1971). Peaking of the T waves can indicate hyponatremia or hyperkalemia (Hori et al., 2006). However, blood electrolytes from these bears were within assumed normal ranges. When peaking of T waves is produced by electrolyte disturbances, the peaking usually is in the form symmetrical peaking or "tenting," whereby the rise and fall of the T wave are similar in duration. That phenomenon was not observed in the brown bear ECGs (Fig. 1).

It is not surprising that the duration of the PQ interval, which is produced principally by the wave of depolarization traversing the head of the AV node, is related to body size in brown bears. Since the muscle fiber types from hearts of different size are dimensionally and physiologically the same, heavier bodies have larger hearts, longer pathways of activation, and therefore longer durations. However, no statistically significant relationships were found between durations of P and QRS versus body weight (Fig. 2). Although heart rates among species are known to vary inversely with body mass (Schmidt-Nielsen, 1984), within-species heart rates appear to be independent of body mass, at least for humans, horses, and dogs (Hamlin, unpubl. data). Concordantly, in bears of this study heart rate did not vary with body size (Fig. 5).

In conclusion, all of the apparent relationships, or lack thereof, may potentially be artifacts of the relatively small numbers of bears studied, particularly when divided into age groups. Given that small bears were younger and body weight was the only physiologic variable that was significantly related to an ECG variable, age may be the factor that obfuscates the relationship between QT and heart rate. Other factors that may have influenced the ECG results include physiologic effects of capture stress, sex, and time of year as it relates to body condition in bears. Despite these unknowns, we are able to conclude that overall the ECGs from brown bears are similar to those of other caniform species. The typical brown bear ECG also shares similarities that are fairly unique to humans, including the concordant orientation of the ST-T vector in the frontal plane with the QRS vector. The ECG is further characterized by peaked T waves and notched QRS complexes. These data add to the base of physiologic references for healthy, free-ranging brown bears.

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