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ARTICLE

Effects of Short-Distance Recreational Mushing on Oxytocin, Gastrin, and Creatinine Kinase in Sled Dogs

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ABSTRACT

A considerable increase in creatinine kinase (CK) activity and gastrin hormone due to exercise has been observed in sled dogs during endurance mushing races; however, there have been no studies on sled dogs during recreational mushing. Although oxytocin hormone is involved in social behaviors and empathy, it has not been studied in sled dogs. This study aimed to assess changes in plasma CK activity, and gastrin and oxytocin concentrations in adult sled dogs used in touristic mushing in North Patagonia, Argentina. Blood samples were collected before, during, and after the winter season of 2017. Creatinine kinase activity measurement was done using an enzymatic assay. Hormone analyses were performed using commercial Enzyme-Linked InmunoSorbent Assay kits. Results showed an expected two-fold increase in CK activity during the winter, with recovering basal values after winter (< 400 UI/L), low and stable levels of gastrin (9.4 ± 8.8 pg/mL), and a slight increase in oxytocin (23%) after mushing activities. No evidence indicated gastrin alterations or muscular damage from touristic mushing, but an oxytocin increase would indicate a stimulation of the brain reward system.

KEYWORDS

Dog condition; oxytocin; gastrin; creatinine kinase

Introduction

The term "mushing" refers to the use of dogs (*Canis lupus familiaris*) for dragging sleds as a mean of transport on snowy surfaces. Sled dogs already existed 9000 years ago (early Holocene) and were domesticated and used by the inhabitants of the Arctic (Pitulko & Kasparov, 2017). In early times, beginning 100 years ago, Alaskan and Siberian sled dogs were bred for one specific purpose: to pull a 180-kg sled with speed and endurance (Iditarod Sled Dog [ISD] Race, 2012). Currently, mushing is used for touristic, sport, and rescue purposes. We are not aware of any studies about the effect of recreational tourism mushing (short races, long rests) on sled dogs. In dogs as well as other mammals, physiological indicators such as hormones and neurotransmitters can be used as a first approach to understanding the animal's condition. In this study, we measured oxytocin and gastrin concentrations as well as creatinine kinase (CK) activity in plasma under different situations in sled dogs before, during, and after mushing activities and during a mushing season.

Oxytocin is a neurohypophysial peptide, and it works as a hormone and neurotransmitter. High oxytocin levels in blood or urine indicates that the brain reward system is active (Mitsui et al., 2011). Oxytocin neuromodulates emotions, behaviors, and cognition processes, crucial factors to achieve social and empathic goals (Ropper & Samuels, 2009), in a way because oxytocin receptors are located in key centers of the central nervous system (Boccia, Petrusz, Suzuki, Marson, & Pedersen, 2013). Oxytocin action is modulated by context and interindividual differences, so to interpret the oxytocin

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response, it is necessary to consider environmental and social factors in designing a study (Olff et al., 2013; Rault, van den Munkhof, & Buisman-Pijlman, 2017).

The antral gastrin hormone (gastrin-17) is one of the dominant gastrin forms (Rehfeld, 1998), and it regulates gastric acid secretion and growth of the gastric mucosa (Rozengurt & Walsh, 2001). Through gastric endoscopy, it was observed that half of racing sled dogs presented gastric lesions after finishing an endurance race (Davis & Williamson, 2016); they even appeared after a single day of long training or a mid-distance race (Williamson et al., 2007; Williamson, Willard, Payton, & Davis, 2010). However, if the exercise was intense but only for a short period, the gastric lesions would be less important (e.g., Davis et al., 2016). In many cases, these gastric pathologies could be asymptomatic (Davis et al., 2003; Dennis et al., 2008; Ritchey et al., 2011), and gastrin measurements might be very useful. In this sense, increases in the antral gastrin hormone could be used as a non-invasive indicator of gastric pathologies as a first approach (Fergestad, Jahr, Krontveit, & Skancke, 2016; Rozengurt & Walsh, 2001). In addition, increased gastrin secretion is usually associated with panic and discomfort in human athletes (de Oliveira & Burini, 2009), and it may be similar in dogs.

The activity of the CK enzyme is commonly used to assess metabolic and functional properties of the cardiac and skeletal muscles (Evans, 2009). Creatinine kinase activity is known to increase with exercise, and sometimes, it could be associated with musculoskeletal damage during training and racing, especially in prolonged endurance sled dog activities (Hinchcliff, Constable, & Di Silvestro, 2004; McKenzie et al., 2007; Piercy et al., 2000). Thus, the increased levels of CK indicate, at least, physical exertion in dogs.

To obtain a first understanding of the dog's condition, this study aimed to assess changes in plasma concentrations of oxytocin and gastrin as well as CK activity in sled dogs due to touristic mushing (tourist excursions) during the winter season in North Patagonia, Argentina.

Materials and methods

Statement pertaining to animal ethics

This research was done in accordance with the Argentine regulations on animal experimentation and the guidelines for animal use described by the *Manual de Buenas Prácticas en la Clínica, la Cirugía y los Diagnósticos Complementarios en la Prestación de Servicios Veterinarios para Animales de Compañía*, approved by the Federación Veterinaria Argentina. The caregivers (owners) of the animals volunteered to participate and gave written informed consent.

Dogs in the study

This study was performed at Chapelco Ski Center (Neuquén province, Argentine Patagonia), where the Bosque de los Huskies has carried out recreational mushing activities during the winter season since 1992. This company owns 63 husky dogs, who are fed two daily servings of high-quality balanced food (Pro Plan® Puppy Complete, Purina®, Santo Tomé, Santa Fe, Argentina), according to body weight and exercise. Information regarding health, training, and feeding routines was collected through questionnaires with the routine veterinary team and breeders.

During the winter season, the dogs make several daily trips around an Andean forest; during these trips, 8 dogs drag the sled with two people (a tourist and a musher) at Mount Chapelco (1600 m above sea level). During the winter season, the average temperatures range from −4.2°C to 5.5°C. The circuit is 5.5 km long and lasts about half an hour. Each dog performs the circuit 5 times to 10 times per day (27.5 km–55 km). At night, they remain in individual boxes (0.8 m tall, 0.8 m wide, and 1.0 m deep) at the mountain. The rest of the year, the dogs reside in a field kennel in 2-m × 2-m × 2-m wired cubicles arranged in pairs. In this study, a group of four- to six-year-old sled dogs (n = 12), including 6 males and 6 females, were studied before, during, and after the winter tourist season of 2017. It was not possible to include a non-exercising group because the company used all the dogs to carry out the mushing activity.

Collecting and storage of blood samples

Blood samples were collected before and after the winter season in the field kennel (May 2017 and September 2017, respectively). Also, blood samples were collected during mushing activities at Chapelco Ski Center during two opportunities, early and late winter (June 2017 and August 2017, respectively). Samples from the ski center were collected shortly before (15 minutes–30 minutes) and immediately after two laps to the mushing circuits (11 km). Collection of samples before mushing occurred at the beginning of the day's activity, or the first two laps of the day. None of the dogs received food in at least the previous 5 hours before sample collection to avoid a food-induced hormone response; they also were not medicated (i.e., gastric acid-reducing agents) prior to blood sampling. The dogs were handled by people who were usually in contact with them, and the samples were collected by the dogs' veterinarian to avoid undesired effects on the hormones and enzyme values. Samples were classified according to the time of sampling into before winter (BW), early winter (W1), late winter (W2), and after winter (AW). Early winter and W2 samples included the samples collected before and after the mushing circuits. The dogs were acclimatized for 25 days to each environment (ski center, field kennel) before sample collection.

Approximately 15 mL of blood samples were obtained from each dog's cephalic vein. Ethylenediaminetetraacetic (EDTA) 0.5 M, pH 8, was added to samples (1 mg/mL blood), and within 1 hour, the samples were centrifuged 1600 *x g* for 15 minutes at 4°C. Plasma was transferred to labeled cryotubes and immediately transported in a cooler and stored at −70°C. This procedure was the same for all sampling events.

Analysis of oxytocin, gastrin, and creatinine kinase

Oxytocin measurement was performed using the Oxytocin Enzyme-Linked InmunoSorbent Assay (ELISA) kit (Enzo Life Science Inc., New York, NY) with a previous peptide extraction using C18 Florisil columns (Burdick & Jackson, Muskegon, MI). The oxytocin analysis is a competitive immunoassay with a rabbit polyclonal antibody to oxytocin. The lower and upper limits of detection are 15.6 pg/mL and 1000 pg/mL, respectively. The manufacturer maximum interassay and intra-assay coefficients of variation (CV) are 20.9% and 13.3%, respectively. Gastrin analysis was performed using the Gastrin 17 ELISA kit (GastroPanel, Helsinki, Finland) based on a sandwich immunoassay with a G-17 specific capture monoclonal antibody. The lower and upper limits of detection are 0.4 pmol/L and 30 pmol/L respectively. The manufacturer interassay and intra-assay CV are less than 8% and 10%, respectively. Both analyses are designed for human measurement but were currently applied for measurement of canine hormones (e.g., Fergestad et al., 2016). Hormone measurements were analyzed using the M201 Microplate Reader (Shenzhen Emperor Electronic Technology Co., LTD, Shenzhen, China). The CK activity analysis was performed using an enzymatic assay (BioSystem S.A., Barcelona, Spain) according to kit instructions and using a Mindray BS-380 analyzer (Mindray Co., Shenzhen, China). The lower and upper limits of detection are 1.92 UI/L and 1300 UI/L, respectively. The manufacturer interassay and intra-assay CV are 1.1% and 3.3%, respectively (using 159 UI/L). For our data, the interassay and intra-assay CVs were ≤ 10%.

Statistical analysis

Data were compiled in Microsoft® Excel (Microsoft Corporation, Redmond, Washington) and were subsequently imported into Statistical Package for the Social Science (SPSS) Version 14.0 (IBM, Chicago, IL). Distribution of oxytocin, gastrin, and CK data was assessed by histograms. Formal tests for normality (Shapiro-Wilks) were also applied. Gastrin and CK variables did not fulfill the normality assumption, and non-parametric analyses were performed. Mann Whitney U tests or one-way analyses of variance (ANOVAs) were used to contrast individual animal and sex differences. To compare the variables among sampling dates (BW, W1, W2, and AW), Friedman tests or

one-way repeated-measures ANOVAs were applied. For these tests, only the data from W1 and W2 samples obtained before the mushing were considered (the effect of mushing was tested in the next tests). To explore the effect of mushing (before vs. after mushing circuits), only the winter season was considered (W1 and W2) using the two-way Friedman or two-way repeated-measures ANOVAs.

Results

Information regarding health, exercise, and feeding routines during the study was considered to be similar for all dogs. All dogs were considered healthy based on physical examination by a veterinarian, and none had clinical signs of gastrointestinal dysfunction or muscular illness according to the owners and veterinary observations. No differences were observed in oxytocin, gastrin, or CK levels between sexes (Table 1).

Oxytocin

Mean oxytocin was 15.0 ± 3.2 pg/mL (± SD), with a range from 10.1 pg/mL to 25.2 pg/mL (median = 15.1 pg/mL). There were no significant differences among individuals in oxytocin levels nor were there differences among sampling dates (Figure 1). Two-way repeated-measures ANOVA indicated a significant increase in oxytocin levels after the sleigh rides ($F = 8.31$, $p < 0.05$; mean increase of 8% in W1 and 23% in W2), and these levels did not significantly differ from W1 to W2 (Figure 2).

Gastrin

The mean gastrin value of sled dogs was 9.4 ± 8.8 pg/mL (± SD) and ranged from 0.2 pg/mL to 52.5 pg/mL (median = 5.2 pg/mL). We found that one female and two males had higher gastrin levels (median = 25.0 pg/mL, 15.4 pg/mL, and 25.5 pg/mL) than the rest of the dogs (medians < 9.8 pg/mL; $X^2 = 42.49$, $p < 10^{-4}$). The gastrin concentration was lower during AW with respect to BW ($X^2 = 8.20$, $p < 0.05$; Figure 1). It decreased after sleigh rides ($X^2 = 7.87$, $p < 0.05$) during both W1 and W2 (Figure 2).

Creatinine kinase

The mean CK was 120 ± 80 UI/L (± SD) and ranged from 5 UI/L to 376 UI/L (median = 103 UI/L). There were no significant differences among individuals in CK levels. There were significant differences among sampling dates, which were higher in W2 than during BW and AW ($X^2 = 8.89$, $p < .05$; Figure 1). Thus, CK increased during winter and recovered its preseason levels after the season. A two-way Friedman test indicated that CK levels did not significantly change by mushing activities, but they increased 35% from W1 to W2 ($X^2 = 6.10$, $p < .05$; Figure 2).

Discussion

Far from the sled dog racing situation, in which teams of 16 dogs and the musher travel 160 km per day for 8 days to 10 days at speeds of 13 km/hour to 21 km/hour (e.g., ISD Race, 2012), sled dogs engaged in recreational mushing at Chapelco Ski Center participated in sleigh rides and ran 75 km per day at 10 km/hour with rest times in the middle and a normal night sleep. Maybe this difference is why recreational mushing represents a minimally stressful

Table 1. Comparison of oxytocin, gastrin, and creatinine kinase (CK) activity between sexes.

		Oxytocin (pg/mL)	Gastrin (pg/mL)	CK (UI/L)
Females	Mean ± SD	14.6 ± 3.1	9.7 ± 9.2	117 ± 82
	Median	14.0	5.9	104
Males	Mean ± SD	15.5 ± 3.4	8.4 ± 9.7	121 ± 72
	Median	15.3	4.6	103

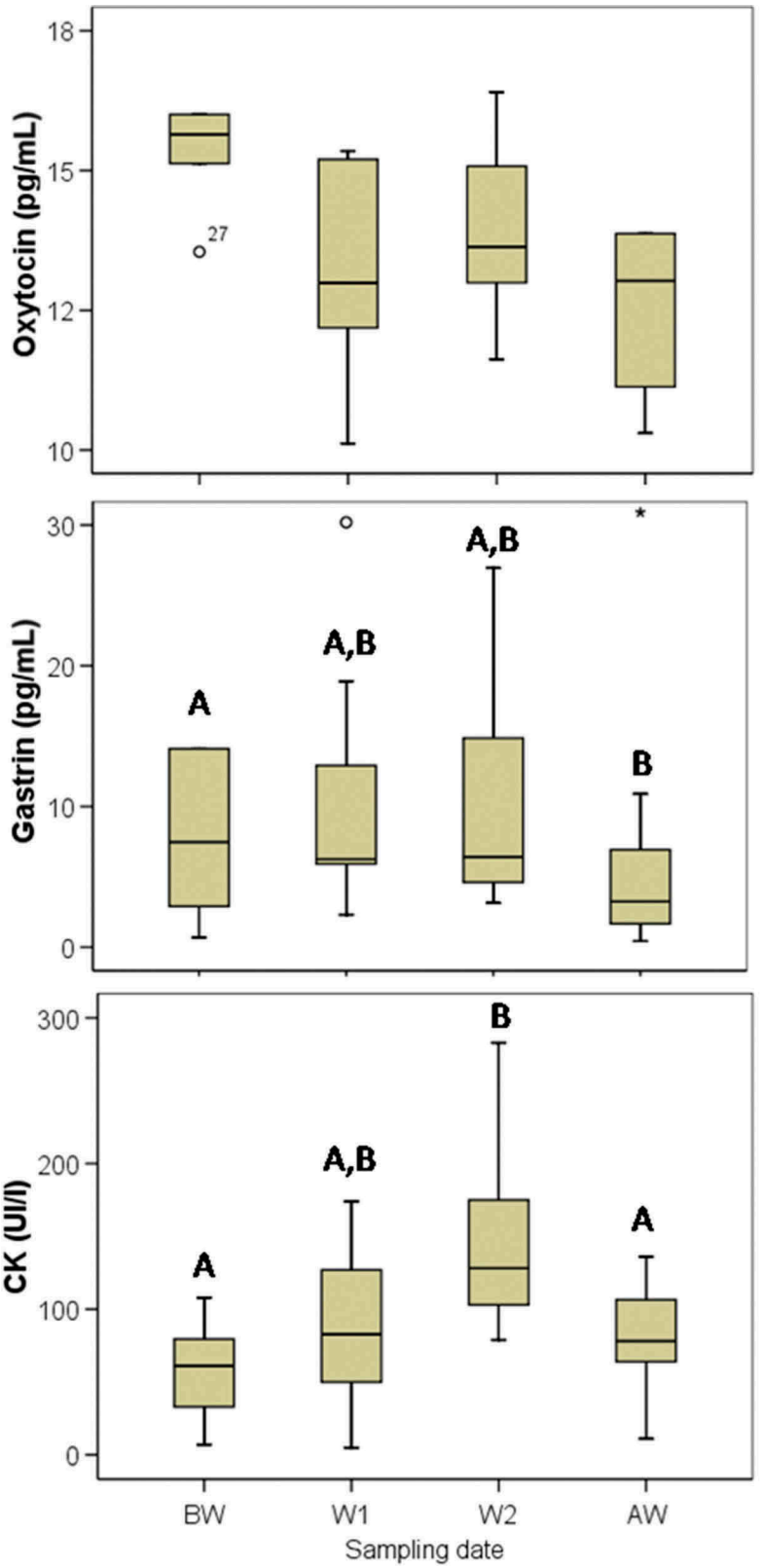

Figure 1. Comparison of oxytocin concentration (pg/mL), gastrin concentrations (pg/mL), and creatinine kinase (CK) activity (UI/L) before winter (BW), during mushing activity season (W1 = early winter, W2 = late winter), and after winter (AW). Letters on the boxes show post-hoc analyses.

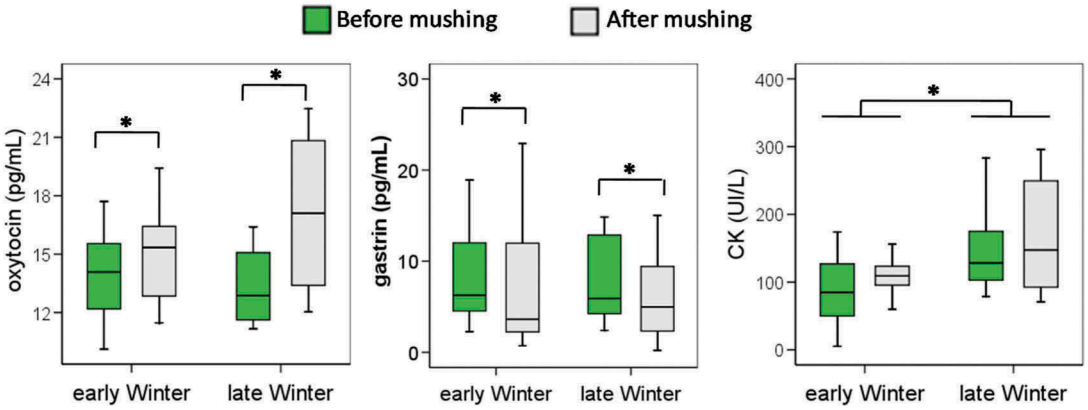

Figure 2. Comparison of oxytocin concentration (pg/mL), gastrin concentrations (pg/mL), and creatinine kinase (CK) activity (UI/L) before and after two mushing trips in early and late winter 2017. Asterisks indicate significant differences.

impact on canine physiology compared with competitive racing. The main findings of this study were that dogs involved in recreational mushing activities had a slight increase in plasma oxytocin, a slight decrease in plasma gastrin, and an expected increase on the CK levels during exercise, with no differences between sexes.

The oxytocin levels slightly increased after the mushing round, which was probably induced not only by mushing exercise per se, but also by praise from the dog handler, removing harnesses, social interaction among dogs, and stroking or grooming. Several studies have shown that oxytocin plays an important role in social positive behaviors like maternal and affiliative behavior in dogs and other mammals (Chen & Sato, 2017; Odendaal & Meintjes, 2003). Its concentrations increase significantly in humans and dogs when these two species interact with social gestures like humans talking softly to a dog, gently stroking a dog with long smooth strokes, or low-key playing with a dog and scratching his or her body and ears (Odendaal & Meintjes, 2003; Petersson et al., 2017). Oxytocin also increases during social behaviors in mammals (Carter, Grippo, Pournajafi-Nazarloo, Ruscio, & Porges, 2008). Thus, the observed slight rise in oxytocin may have been induced not only by the race, but also by social interaction with dog handlers and other dogs. Further experiments are needed to evaluate if basal oxytocin is higher in dogs who perform mushing activities than those who do not. For instance, it has been proposed that basal oxytocin concentrations are higher in animals on farms who are reared in natural conditions and in a comfortable environment compared with those in artificial rearing systems (Chen & Sato, 2017). Furthermore, we expect to expand this study in the following years and increase the number of animals sampled to assess if this modest hormone's response varies.

In the present study, gastrin levels of only three dogs were similar to those of huskies with normal exercise in other studies (18.1 ± 8.5 pg/mL, 20.5 ± 12.5 pg/mL; Fergestad et al., 2016), while the gastrin levels of the other nine dogs were lower. Differences among individuals can be attributed to intrinsic individual differences or the clue of an atypical gastric condition at the time of the study, and this finding should be evaluated with other methods.

Previous studies on sled dogs have detected an exercise-induced increase in the serum concentration of gastrin during long-distance mushing races (600 km long), and these concentrations have reached levels of 71 pg/mL to 120 pg/mL (e.g., Fergestad et al., 2016). Those gastrin rises may be related to an increase in the number of gastrin-secreting enteroendocrine cells (G cells) in the antral mucosa, which can lead to gastric dysfunctions (Sun, Song, Cheng, Zhao, & Yao, 2002), such as the breakdown of the mucosal barrier or hyperacidity, as proposed in Alaskan sled dogs (Davis & Williamson, 2016; Williamson et al., 2007, 2010) and retriever dogs (Davis et al., 2016). Thus, gastrin

increases could be correlated with gastric diseases and hormonal imbalances. In contrast, gastrin concentration slightly decreased after recreational mushing slides during winter, and it decreased from BW to AW. These results suggest a low likelihood of gastric disease related to gastrin and also a similar regulation of blood gastrin during rest seasons and recreational mushing. It is possible that regular functions of somatostatin could have remained and limited both the gastric acid release protecting against ulceration and the inhibition of gastrin glomerular filtration in the kidney, as was observed in dogs and other mammals (El Munshid, Håkanson, Liedberg, Rehfeld, & Sundler, 1980; Lloyd, Amirmoazzami, Friedik, Chew, & Walsh, 1997; Vora et al., 1986). Despite these approaches, causes of exercise-induced gastrin levels are complex and unclear and therefore require further study.

To evaluate the degree of musculoskeletal damage in dogs, the assessment of CK activity is widely used (Frank et al., 2015). A modest elevation in plasma or serum CK activity post-exercise is considered to be expected in dogs, particularly under the reference limit value of 400 UI/L (Willard & Tvedten, 2012). Although a substantial increase in CK is insufficient to diagnose clinical or histological evidence of muscle damage or wasting, sometimes, its increase could be associated with muscle efforts and pathologies (e.g., rhabdomyolysis) during prolonged-endurance sled dog races (Hinchcliff et al., 2004; Nance & Mammen, 2015), during which CK achieved values of 336 UI/L to 441,000 UI/L (McKenzie et al., 2007; Piercy et al., 2001). These CK levels far exceed the reference limits. In contrast, induced CK activity during recreational mushing was less prominent than during endurance racing. Creatinine kinase levels did not exceed the reference limits and ranged from 5 UI/L to 376 UI/L with a mean CK activity of 116 UI/L. This finding may suggest a low likelihood of pathologies associated not only with exercise-induced muscle damage and rhabdomyolysis, but also with myocardial damage or arterial obstructions (Burgener, Kovacevic, Mauldin, & Lombard, 2006; Lake-Bakaar, Johnson, & Griffiths, 2012; Thompson, Bragg, & West, 1990).

Creatinine kinase levels were measured shortly before and immediately after recreational mushing, which deserves some consideration. In untrained beagle dogs, a 1-hour race led to CK releasing in the blood, and these levels peaked 4 hours to 6 hours later with baseline values recovering after 24 hours (Chanoit, Concordet, Lefebvre, Orcel, & Braun, 2002). Hence, despite the fact that huskies from this study were trained, it is certainly possible that measured pre-exercise CK levels include leftover levels from the previous day of exercise. Also, because the two laps of mushing lasted approximately 2 hours, measured post-exercise CK levels might represent the ascending curve of CK but not necessarily the peak value. Finally, the decrease in CK from baseline to after the mushing season suggests complete muscle recovery after mushing activities.

Conclusions

This research presents a first attempt to study the status of recreational sled dogs and their physiological condition. The study revealed a mild induction of oxytocin during recreational mushing, without evidence of gastric stress or muscle-related damage. These responses would likely be similar in other mushing activities with a similar diet, care, and exercise style/duration. This research has generated new knowledge on exercise-induced stress and metabolic changes suggesting potential benefits to recreational distance or sprint mushing that warrant further research in the area of oxytocin biology.

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References

Boccia, M. L., Petrusz, P., Suzuki, K., Marson, L., & Pedersen, C. A. (2013). Immunohistochemical localization of oxytocin receptors in human brain. *Neuroscience*, *253*, 155–164.

Burgener, I. A., Kovacevic, A., Mauldin, G. N., & Lombard, C. W. (2006). Cardiac troponins as indicators of acute myocardial damage in dogs. *Journal of Veterinary Internal Medicine*, *20*, 277–283.

Carter, C. S., Grippo, A. J., Pournajafi-Nazarloo, H., Ruscio, M. G., & Porges, S. W. (2008). Oxytocin, vasopressin and sociality. *Progress in Brain Research*, *170*, 331–336.

Chanoit, G. P., Concordet, D., Lefebvre, H. P., Orcel, K., & Braun, J. P. (2002). Exercise does not induce major changes in plasma muscle enzymes, creatinine, glucose and total proteins concentrations in untrained beagle dogs. *Transboundary and Emerging Diseases*, *49*(4), 222–224.

Chen, S., & Sato, S. (2017). Role of oxytocin in improving the welfare of farm animals - A review. *Asian-Australasian Journal of Animal Sciences*, *30*(4), 449–454.

Davis, M. S., Willard, M. D., Day, M. J., Mccann, J., Payton, M. E., & Cummings, S. L. (2016). Effect of exercise on gastric health in field retrievers. *Comparative Exercise Physiology*, *12*(1), 35–39.

Davis, M. S., Willard, M. D., Nelson, S. L., Mandsager, R. E., McKiernan, B. S., Mansell, J. K., & Lehenbauer, T. W. (2003). Prevalence of gastric lesions in racing Alaskan sled dogs. *Journal of Veterinary Internal Medicine*, *17*, 311–314.

Davis, M. S., & Williamson, K. K. (2016). Gastritis and gastric ulcers in working dogs. *Frontiers in Veterinary Science*, *3*, 30.

de Oliveira, E. P., & Burini, R. C. (2009). The impact of physical exercise on the gastrointestinal tract. *Current Opinion in Clinical Nutrition & Metabolic Care*, *12*, 533–538.

Dennis, M. M., Nelson, S. N., Cantor, G. H., Mosier, D. A., Blake, J. E., & Basaraba, R. J. (2008). Assessment of necropsy findings in sled dogs that died during Iditarod Trail sled dog races: 23 cases (1994-2006). *Journal of the American Veterinary Medical Association*, *232*, 564–573.

El Munshid, H. A., Håkanson, R., Liedberg, G., Rehfeld, J. F., & Sundler, F. (1980). Importance of the kidneys for gastrin elimination and gastric function. *The Journal of Physiology*, *299*, 157–171.

Evans, G. O. (2009). *Animal clinical chemistry: A practical handbook for toxicologists and biomedical researchers* (2nd ed.). Minden, NV: CRC Press.

Fergestad, M. E., Jahr, T. H., Krontveit, R. I., & Skancke, E. (2016). Serum concentration of gastrin, cortisol and C-reactive protein in a group of Norwegian sled dogs during training and after endurance racing: A prospective cohort study. *Acta Veterinaria Scandinavica*, *58*(1), 24.

Frank, L., Mann, S., Johnson, J., Levine, C., Downey, R., Griffits, C., & Wakshlag, J. (2015). Plasma chemistry before and after two consecutive days of racing in sled dogs: Associations between muscle damage and electrolyte status. *Comparative Exercise Physiology*, *11*(3), 151–158.

Hinchcliff, K. W., Constable, P. D., & Di Silvestro, R. A. (2004). Muscle injury and antioxidant status in sled dogs competing in a long-distance sled dog race. *Comparative Exercise Physiology*, *1*(1), 81–85.

ISD Race (Iditarod Sled Dog Race). (2012). *Cell*, *148*(5), 839–841.

Lake-Bakaakr, G. A., Johnson, E. G., & Griffiths, L. G. (2012). Aortic thrombosis in dogs: 31 cases (2000–2010). *Journal of the American Veterinary Medical Association*, *241*(7), 910–915.

Lloyd, K. C., Amirmoazzami, S., Friedik, F., Chew, P., & Walsh, J. H. (1997). Somatostatin inhibits gastrin release and acid secretion by activating sst2 in dogs. *American Journal of Physiology-Gastrointestinal and Liver Physiology*, *272*, G1481–G1488.

McKenzie, E. C., Jose-Cunilleras, E., Hinchcliff, K. W., Holbrook, T. C., Royer, C., Patyon, M. E., … Nelson, S. (2007). Serum chemistry alterations in Alaskan sled dogs during five successive days of prolonged endurance exercise. *Journal of American Veterinary Medical Association*, *230*, 1486–1492.

Mitsui, S., Yamamoto, M., Nagasawa, M., Mogi, K., Kikusui, T., Ohtani, N., & Ohta, M. (2011). Urinary oxytocin as a non invasive biomarker of positive emotion in dogs. *Hormones and Behavior*, *60*, 239–243.

Nance, J. R., & Mammen, A. L. (2015). Diagnostic evaluation of rhabdomyolysis. *Muscle Nerve*, *51*(6), 793–810.

Odendaal, J. S., & Meintjes, R. A. (2003). Neurophysiological correlates of affiliative behaviour between humans and dogs. *The Veterinary Journal*, *165*(3), 296–301.

Olff, M., Frijling, J. L., Kubzansky, L. D., Bradley, B., Ellenbogen, M. A., Cardoso, C., … van Zuiden, M. (2013). The role of oxytocin in social bonding, stress regulation and mental health: An update on the moderating effects of context and interindividual differences. *Psychoneuroendocrinology*, *38*, 1883–1894.

Petersson, M., Uvnäs-Moberg, K., Nilsson, A., Gustafson, L. L., Hydbring-Sandberg, E., & Handlin, L. (2017). Oxytocin and cortisol levels in dog owners and their dogs are associated with behavioral patterns: An exploratory study. *Frontiers in Psychology*, *8*, 1796.

Piercy, R. J., Hinchcliff, K. W., DiSilvestro, R. A., Reinhart, G. A., Baskin, C. R., Hayek, M. G., … Swenson, R. A. (2000). Effect of dietary supplements containing antioxidants on attenuation of muscle damage in exercising sled dogs. *American Journal of Veterinary Research*, *61*(11), 1438–1445.

Piercy, R. J., Hinchcliff, K. W., Morley, P. S., Di Silvestro, R. A., Reinhart, G. A., Nelson, Jr, S. L., … Craig, A. M. (2001). Vitamin E and exertional rhabdomyolysis during endurance sled dog racing. *Neuromuscular Disorders*, *11* (3), 278–286.

Pitulko, V. V., & Kasparov, A. K. (2017). Archaeological dogs from the Early Holocene Zhokhov site in the Eastern Siberian Arctic. *Journal of Archaeological Science: Reports*, *13*, 491–515.

Rault, J. L., van den Munkhof, M., & Buisman-Pijlman, F. T. A. (2017). Oxytocin as an indicator of psychological and social well-being in domesticated animals: Acritical review. *Frontiers in Psychology*, *8*, 1521.

Rehfeld, J. F. (1998). The new biology of gastrointestinal hormones. *Physiological Reviews*, *78*, 1087–1108.

Ritchey, J. W., Davis, M. S., Breshears, M. A., Willard, M. D., Williamson, K. K., Royer, C. M., … Cragun, A. S. (2011). Gastritis in Alaskan racing sled dogs. *Journal of Comparative Pathology*, *145*, 68–76.

Ropper, A., & Samuels, M. (2009). The hypothalamus and neuroendocrine disorders. In A. Ropper & M. Samuels (Eds.), *Adams and victor's principles of neurology*. New York, NY: McGraw-mountain.

Rozengurt, E., & Walsh, J. H. (2001). Gastrin, CCK, signaling, and cancer. *Annual Review of Physiology*, *63*, 49–76.

Sun, F. P., Song, Y. G., Cheng, W., Zhao, T., & Yao, Y. L. (2002). Gastrin, somatostatin, G and D cells of gastric ulcer in rats. *World Journal of Gastroenterology*, *8*, 375–378.

Thompson, J. S., Bragg, L. E., & West, W. W. (1990). Serum enzyme levels during intestinal ischemia. *Annals of Surgery*, *211*(3), 369–373.

Vora, J. P., Owens, D. R., Ryder, R., Atiea, J., Luzio, S., & Hayes, T. M. (1986). Effect of somatostatin on renal function. *British Medical Journal (Clinical Research Ed.)*, *292*, 1701–1702.

Willard, M. D., & Tvedten, H. (2012). *Small animal clinical diagnosis by laboratory methods* (5th ed.). St. Louis: Elsevier.

Williamson, K. K., Willard, M. D., McKenzie, E. C., Royer, C. M., Payton, M. E., & Davis, M. S. (2007). Efficacy of famotidine for the prevention of exercise-induced gastritis in racing Alaskan sled dogs. *Journal of Veterinary Internal Medicine*, *21*, 924–927.

Williamson, K. K., Willard, M. D., Payton, M. E., & Davis, M. S. (2010). Efficacy of omeprazole versus high-dose famotidine for prevention of exercise-induced gastritis in racing Alaskan sled dogs. *Journal of Veterinary Internal Medicine*, *24*, 285–288.