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Kinematic analysis of the gait of adult sheep during treadmill locomotion: Parameter values, allowable total error, and potential for use in evaluating spinal cord injury

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ABSTRACT

We are developing a novel intradural spinal cord (SC) stimulator designed to improve the treatment of intractable pain and the sequelae of SC injury. In-vivo ovine models of neuropathic pain and moderate SC injury are being implemented for pre-clinical evaluations of this device, to be carried out via gait analysis before and after induction of the relevant condition. We extend previous studies on other quadrupeds to extract the three-dimensional kinematics of the limbs over the gait cycle of sheep walking on a treadmill. Quantitative measures of thoracic and pelvic limb movements were obtained from 17 animals. We calculated the total-error values to define the analytical performance of our motion capture system for these kinematic variables. The post- vs. pre-injury time delay between contralateral thoracic and pelvic-limb steps for normal and SC-injured sheep increased by ~24 s over 100 steps. The pelvic limb hoof velocity during swing phase decreased, while range of pelvic hoof elevation and distance between lateral pelvic hoof placements increased after SC injury. The kinematics measures in a single SC-injured sheep can be objectively defined as changed from the corresponding pre-injury values, implying utility of this method to assess new neuromodulation strategies for specific deficits exhibited by an individual.

1. Introduction

Our laboratories are developing the Human Spinal Cord Modulation System (HSCMS) as a novel means of intradural spinal cord stimulation (SCS). In this approach, the electrode array is placed directly on the pial surface of the spinal cord [3], in contrast to the present standard practice in which the stimulator contact is placed in the epidural space. The primary motivation for intradural placement of the array is that it enables more selective excitation and deeper penetration of the target neural tissues, in part by overcoming the electrical shunting effects caused by the high conductivity of the cerebrospinal fluid [15]. That capability should provide improved treatment of patients suffering from intractable pain and, possibly, for those with lower-limb spasticity and other motor control problems arising from spinal cord injury (SCI).

For successful implementation of intradural placement, the electrode array must be designed to remain in stable, gentle contact with the pial surface of the spinal cord as it moves within the thecal sac during flexion and extension of the vertebral column. The HSCMS has been designed with biomechanical characteristics that are compatible with this requirement, and the technical aspects of its performance have been tested extensively [18,25]. The next step in the development cycle calls for implantation of a fully functional prototype in an in vivo model of chronic intradural spinal cord stimulation [20]. Sheep were chosen for this work primarily because their large spinal cord size makes them a useful anatomical surrogate for humans [8,19]. Moreover, their electrophysiological characteristics have been studied extensively and are appropriate for stimulation-based measurements of somatosensory evoked potentials and single-unit neuronal recordings [5,6]. Lastly, because of their flexible cervical vertebral columns, these animals serve as an excellent in vivo test bed for evaluating the electromechanical robustness of the HSCMS leads [22].

In order to investigate how ovine models of chronic neuropathic pain and moderate spinal cord injury respond to spinal cord stimulation as delivered by the HSCMS, we have chosen to employ image-based gait analysis during treadmill walking. Part of the motivation for doing this was that video-based observations of quadrupeds with spinal cord

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injury walking on treadmills has led to subtle measures of the effects of therapeutic interventions in other species such as dogs [9]. We therefore hypothesize that injury models, either without or with spinal cord stimulation, will affect kinematics of step cycle timing between thoracic and pelvic limb, flexion and extension of pelvic limb joints and range of hoof elevation during treadmill walking. As the first step in this study, we here outline the kinematic parameters of gait pattern of thoracic and pelvic limbs and temporospatial measures of hock (ankle) joint angle in the sagittal plane (leg swing angle) in clinically healthy adult sheep (n = 17). We also demonstrate the accuracy of measurements in detection of differences between naïve and injured states within an individual sheep. Through measurement of total error of our analytical system we illustrate the high sensitivity of this system to detect changes in gait measures induced by injury in an individual animal. These findings highlight the applicability of the method in future studies that evaluate the effects of electrical stimulation or other interventions on outcome in individual animals or people.

2. Materials and methods

2.1. Experimental animals and preparations

This investigation was approved by the Institutional Animal Care and Use Committees (IACUC) of Iowa State University (ISU), Ames, IA, USA (IACUC Approval No. 2-12-7298-O) and the University of Iowa, Iowa City, IA, USA (IACUC Approval No. 1308149) where the surgical component of the work was done. A total of 18 adult (four male and 14 female; Polypay and Suffolk) sheep (*Ovis aries*) were used in this study. The sheep were ~70 kg weight and ~2 years of age. Upon delivery, each animal was examined by a veterinarian and deemed non-pregnant and free of disease. The animals were normally kept at the Laboratory Animal Resources Facility of Iowa State University and fed a diet consisting of hay supplemented with concentrate according to their requirements, and had free access to fresh water. Throughout the study, all experimental animals were monitored and maintained in good health. Data collection and analysis were carried out at the Motion Analysis Laboratory in the College of Veterinary Medicine of Iowa State University. A single sheep, with an incomplete spinal cord injury at T8, produced by dropping a 50 g weight with 4 mm diameter tip through 10 cm, similar to techniques used by other researchers in various species [1,16,28], was used to investigate the differences in kinematic patterns and measures of gait before and 12 weeks after injury.

2.2. Experimental arrangement

Upon initial delivery to ISU, each of the sheep was trained for gait analysis. Briefly, each sheep was led, using a halter, onto the stationary treadmill belt (EB730, Ephrata, PA, GoPetUSA). They were then allowed time to habituate to the environment and offered food rewards. The treadmill belt was started at the slowest speed possible and then increased in small increments over a period of about 5 min. The top speed required for this testing was equivalent to the normal walking pace for an adult human (3.75 km/h). Two factors governed this choice: (1) the speed should not be so high that it forced the animal to trot rather than walk to keep up with the treadmill, and (2) the speed should not be so slow that the animal had time to pause intermittently and yet still maintain pace with the treadmill belt. The desired end-result was that the sheep would walk at a constant, comfortable pace on treadmill. If a sheep showed signs of distress, such as resistance to walking, the treadmill was stopped to allow time out to calm for a few minutes before starting again. If a sheep showed undue signs of stress when re-introduced to the treadmill on a second occasion, such as backing away and attempting to jump, it was returned to the home pen and acclimatization commenced again the following day. It generally took about 30–45 min for each sheep to become accustomed to the procedure, although the acclimatization period was usually achieved during six to ten sessions over a two to three week period, so that they would approach the treadmill and walk without hesitation. During the data collection periods, care was taken to ensure that each sheep maintained a steady walking gait, using visual judgment of comfort and lack of resistance as a means of having habituated animals. Because all the sheep were of the same range of size and weight, the target speed of 3.75 km/h was set for the whole cohort.

2.3. Data acquisition

The details of the multi-camera video imaging system and motion analysis package are provided elsewhere [22]. Briefly, the six infrared cameras (three cameras on each side of the animal) of a motion analysis system (Vicon Motion Systems Ltd., Oxford, UK) operating at frame rates of 100 Hz were used to monitor the trajectories of 14 mm diameter optical markers. These markers were attached on all four hooves and various locations (mentioned below) on the skin of all the animals using adhesive fasteners (Velcro USA Inc., Manchester, NH, US) (Fig. 1). To prepare the skin for easier attachment of the markers, the sheep were sheared before the recording day. The motion of the hock (tarsal/tarsus) joint was defined using three markers attached by the same person to each of the tibial and metatarsal regions, as also shown in Fig. 1. Briefly, and in addition to the markers attached to the cranio-lateral edge of hooves, hock joint upper and lower segments consisted of three markers each. The hock joint upper segment was created by

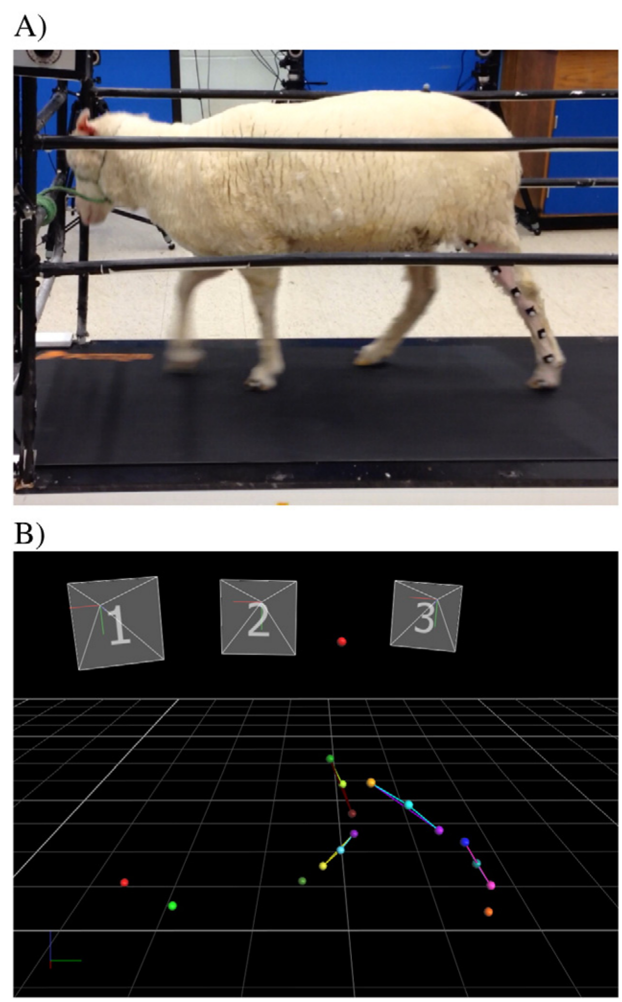

Fig. 1. A) Ovine model undergoing gait training on the treadmill system. The infrared reflective markers used for video tracking purposes can be seen on the animal's left pelvic limb. B) Ovine 3D model created by 17 infrared reflective markers and video captured by total of six cameras, three on each side of animal on the treadmill system.