ARTICLE IN PRESS

Journal of Biomechanics xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Journal of Biomechanics

journal homepage: www.elsevier.com/locate/jbiomech
www.JBiomech.com

Uncovering the structure of the mouse gait controller: Mice respond to substrate perturbations with adaptations in gait on a continuum between trot and bound

A. Vahedipour[a,1,*], O. Haji Maghsoudi[a], S. Wilshin[b], P. Shamble[a,2,3], B. Robertson[a,4], A. Spence[a]

[a] *Department of Bioengineering, Temple University, Philadelphia, PA 19122, USA*
[b] *Structure and Motion Laboratory, Royal Veterinary College, University of London, London, United Kingdom*

ARTICLE INFO

Article history:
Accepted 9 July 2018
Available online xxxx

Keywords:
Gait
Perturbation
Bounding
Mice
Treadmill

ABSTRACT

Animals, including humans, have been shown to maintain a gait during locomotion that minimizes the risk of injury and energetic cost. Despite the importance of understanding the mechanisms of gait regulation, ethical and experimental challenges have prevented full exploration of these. Here we present data on the gait response of mice to rapid, precisely timed, spatially confined mechanical perturbations. Our data elucidate that after the mechanical perturbation, the mouse gait response is anisotropic, preferring deviations away from the trot towards bounding, over those towards other gaits, such as walk or pace. We quantified this shift by projecting the observed gait onto the line between trot and bound, in the space of quadrupedal gaits. We call this projection λ. For $\lambda = 0$, the gait is the ideal trot; for $\lambda = \pm\pi$, it is the ideal bound. We found that the substrate perturbation caused a significant shift in λ towards bound during the stride in which the perturbation occurred and the following stride (linear mixed effects model: $\Delta\lambda = 0.26 \pm 0.07$ and $\Delta\lambda = 0.21 \pm 0.07$, respectively; random effect for animal, $p < 0.05$ for both strides, n = 8 mice). We hypothesize that this is because the bounding gait is better suited to rapid acceleration or deceleration, and an exploratory analysis of jerk showed that it was significantly correlated with λ ($p < 0.05$). Understanding how gait is controlled under perturbations can aid in diagnosing gait pathologies and in the design of more agile robots.

1. Introduction

Locomotion is critical to survival and reproduction in most animals. A critical feature of successful locomotion is selection and maintenance of gait. While it has been shown that animals, including humans, choose gaits that appear to minimize energy consumption and injury risk (Hoyt and Taylor, 1981; Farley and Taylor, 1991), a large amount of variability exists in gait selection across animals (Hildebrand, 1989), and across conditions, such as treadmill (Blaszczyk and Loeb, 1993) or rough terrain (Wilshin et al., 2017a). Further, animals make fluid transitions between gaits; yet we have little understanding of how factors such as the mechanics of the different gaits influence these transitions (Ijspeert et al., 2007; Haynes and Rizzi, 2006).

Individuals often encounter perturbations during normal locomotion, from which they have to recover. Perturbations can also be used as a tool by an experimenter to elucidate mechanisms that are not observable in steady state conditions, and to better refine mathematical models, especially in the field of gait rehabilitation and robotics (Komura et al., 2005; Schmidt et al., 2005). Despite the utility of perturbation experiments both as a naturalistic stimulus and as a probe of control structure, ethical and experimental challenges have prevented full exploration of these in legged systems.

Biological studies utilizing perturbations of moving animals have lead to improvements in robots (Altendorfer et al., 2001; Haynes et al., 2009), given insight into basic locomotor biomechanics (Jindrich and Full, 2002; Daley et al., 2006), and improved understanding of disease and injury in humans (Lamontagne et al., 2007;

---

* Corresponding author at: Department of Bioengineering, Engineering Building Room 819, College of Engineering, Temple University, 1947 N. 12th Street, Philadelphia, PA 19122, USA.

E-mail address: annie.vahedipour@yale.edu (A. Vahedipour).

[1] Current address: Department of Pediatric Neurology, Yale School of Medicine, 333 Cedar Street, New Haven, CT 06510, USA.

[2] Current address: John Harvard Distinguished Science Fellowship Program, Harvard University, Cambridge, MA 02138, USA.

[3] Current address: Department of Organismic and Evolutionary Biology, Harvard University, Cambridge, MA 02138, USA.

[4] Current address: Edgewise Therapeutics, Boulder, CO 80303, USA.

https://doi.org/10.1016/j.jbiomech.2018.07.020
0021-9290/© 2018 Elsevier Ltd. All rights reserved.

Please cite this article in press as: Vahedipour, A., et al. Uncovering the structure of the mouse gait controller: Mice respond to substrate perturbations with adaptations in gait on a continuum between trot and bound. J. Biomech. (2018), https://doi.org/10.1016/j.jbiomech.2018.07.020

Protas et al, 2005). For instance, Gritsenko et al. (2001) studied the role of muscle activity and latency response of cats to unexpected perturbation before and after unilateral denervation of synergists. De Leon et al. (2000) also studied the relationship between the force control in flexor motor pools and adaptation to spinal cord injury in rats using gait perturbations. Similar studies have been carried out to analyze trained compensatory postural responses in older human adults during perturbed treadmill locomotion (Shapiro and Melzer, 2010). However, we have not found prior work that examines in detail the changes in gait by rodents in response to an unexpected mechanical perturbation. Characterizing such responses in rodents is important as they are becoming increasingly popular model systems in locomotion studies (Talpalar and Kiehn, 2010; Bellardita and Kiehn, 2015; Harris-Warrick, 2011), they provide a wide array of disease models (Rosenthal and Brown, 2007), and offer a wide range of genetic tools to manipulate aspects of both the neuro- and more general physiology (Lathe, 1996). Thus, here we examine the gait response of intact, freely running mice to a mechanical substrate perturbation.

Based on recent results in dogs walking on rough terrain (Wilshin et al., 2017a), where perturbed gait at walking speeds was found to be restricted along the walk-trot line, it could be hypothesized that a similar anisotropy would exist at trot: e.g., that mice will exhibit perturbed gait around trot on the line between trot and walk. However, the consideration for quasi-static stability that predicted the result in walking dogs is less likely to apply at the trotting speeds commonly used by rodents. Therefore it is unclear how to make a similar *a priori* prediction for the structure around trot without a model of dynamic stability that can be incorporated into our gait analysis framework. We therefore carried out the following exploratory study of mouse gait control about the trot.

2. Materials and methods

A computer vision controlled treadmill system capable of applying rapid, precisely timed, and spatially confined mechanical perturbations to freely running mice was the central piece of apparatus (Fig. 1).

2.1. Materials

2.1.1. Animals

Eight adult female C57BL/6J mice were used in this study (http://jaxmice.jax.org/strain/013636.html). Animals were housed under a 12:12 h light–dark cycle in a temperature-controlled environment with food and water available *ad libitum*. Animal procedures were approved by the Temple University Institutional Animal Care and Use Committee ACUP #4675.

2.1.2. Treadmill-Camera system

We used a video-tracking, closed-loop treadmill system to control perturbation application and improve yield. The system employs a real-time feed of the position and speed of the mouse to adjust the belt speed (Spence et al., 2013). The system is built upon a Panlab Model Number LE8700 treadmill. Two cams, in the shape of ½ of a disk, were machined and mounted on a shaft, running beneath the treadmill surface, under the belt. Slots cut in the belt support surface allowed these cams to push upward and deflect the surface. These cams produced small "earthquakes" (Fig. 1). To achieve fast motor response times, the motors and control system for the substrate deflection and the treadmill belt were essentially a two-legged version of the X-RHex robot (Haynes et al., 2012), where treadmill functionality replaced legged robot code.

The real-time feed was further used to trigger the mechanical perturbations, randomized between the left and right sides of the belt. We randomized the side of perturbation because in preliminary experiments we found that mice quickly learned which side of the treadmill contained the perturbation and would avoid it. This "behavioral triggering" based on the feed of animal position and speed can minimize the confounding effects due to variation in quantities such as speed, acceleration, and/or position relative to the earthquake. The perturbation was automatically triggered if the mice were running continuously for at least 0.75 sec, with a speed between 0.2 and 0.5 m/s (Video S1). An average-weight mouse of 30 g has a preferred speed of 0.46 m/s and trots in the range of 0.19–0.67 m/s (Spence et al., 2013; Herbin et al., 2004). A custom five camera high-speed video system was used to gather the kinematic data. For three of the mice an earlier version of the system consisting of two mirrors and two cameras, one for the real-time feed and the other for recording high-speed videos, was used, as described in Spence et al., 2013.

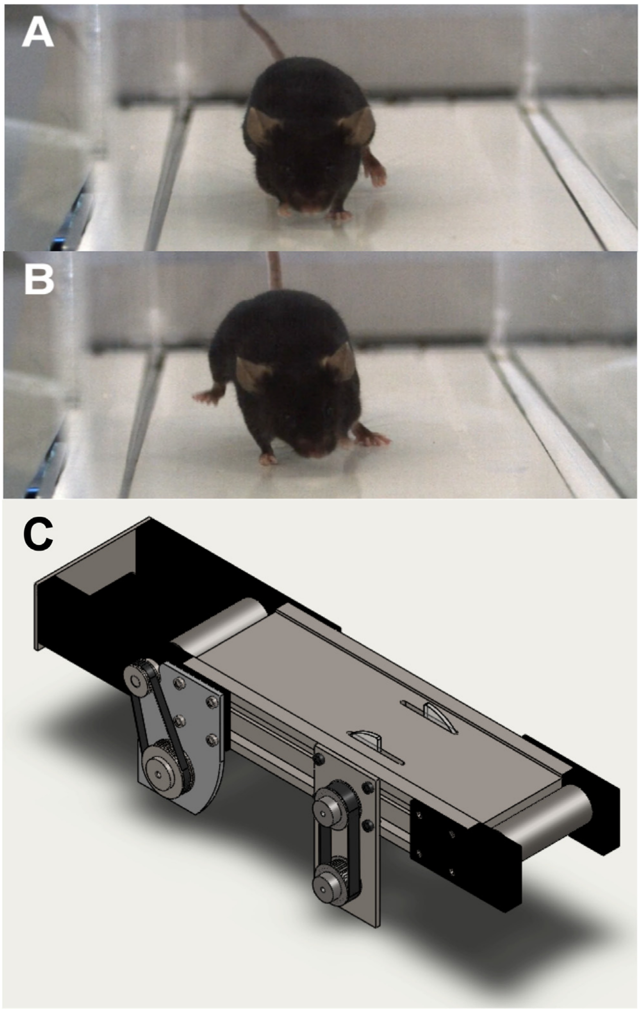

Fig. 1. (A) Intact, running mice before, and (B) after applying perturbation. (C) Rendering of the treadmill, including the two perturbation disks.

2.2. Experimental design

2.2.1. Animal training

All mice were trained daily (M-Th) for 2 weeks to run on the treadmill prior to collecting data. The first week of training session consisted of 10 min treadmill acclimation, with access to food rewards, before and after activating the treadmill, followed by 15 min of running on the treadmill. On the second week of train-

Please cite this article in press as: Vahedipour, A., et al. Uncovering the structure of the mouse gait controller: Mice respond to substrate perturbations with adaptations in gait on a continuum between trot and bound. J. Biomech. (2018), https://doi.org/10.1016/j.jbiomech.2018.07.020