Aging and Instability: A Macaque Model for Normal Distribution of Plantar Mechanoreceptors

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Research Questions

1. How do Meissner corpuscles (MC) and Pacinian corpuscles (PC) distributions vary across regions of the plantar foot in rhesus macaques (*Macaca mulatta*) in relation to functional demands?
2. How do these distributions compare to human mechanoreceptor distributions?

Introduction

Importance of the Plantar Foot: Plays a vital role in balance and stability during movement.

Mechanoreceptor Function:
- MCs (**Fig. 1a)** and PCs (**Fig. 1b)** provide somatosensory feedback critical for locomotion

Impact of Aging:
Age-related mechanoreceptor decline reduces tactile sensitivity
- Increased risk of falls and balance-related injuries

Model for Aging Research:
- Rhesus macaques serve as a valuable model for studying human aging.

Study Focus:
- Identify MC and PC distributions in the foot of healthy adult macaques and compare with published human data.

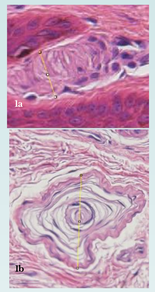

Fig 1 (a) Meissner corpuscle
(b) Pacinian corpuscle

Approach

Rhesus macaque model:
- Semi-terrestrial/arboreal quadrupeds with grasping feet
- Long lifespans (1/3 the length of humans)
- Commonly used to study sensory anatomy and aging.
- Similar to humans, they exhibit increased representation of hands and fingers relative to feet and toes in the somatosensory cortex
- Free-range population at Cayo Santiago Primate Field Station in Costa Rica

Figure 2: Rhesus macaque on a branch of a tree

What'd We Expect?

Hypotheses:

1. Mechanoreceptor distributions in both species will differ between the heel and toes due to functional roles in locomotion.
2. Human and macaque distributions will vary due to bipedal vs. quadrupedal locomotion.

Methodology

Sample Collection

Study Location:
- Samples collected opportunistically during necropsies

Subjects:
- Six young adults (3 males and 3 females).

Sampling Sites: (Fig. 3)

Histological Analysis:
- 6-7 5 um thick sections, 100 um apart
- Sections stained with H&E. (**Fig. 4a**)
- Quantified section lengths and average MC and PC counts and size across sections to calculate density (**Fig 4b & 4c)**

Human data:
- MC and PC densities were not available for human feet, so we used published innervation densities of FAI (MC) and FAII (PC) fibers (**Ref 2**)

Fig. 3. Sample sites that were taken from the feet of macaques

Statistical Analysis

- We used linear mixed effects models to test for an effect of sampling site on MC and PC density in the macaque foot, controlling for individual identity and sex (R package *Lme4*)
- We performed post-hoc paired comparisons to test for specific differences between sampling sites using a Tukey p-value adjustment (*R* package *emmeans*)

Fig 4 (a) Measurement taken of the entire H&E sample

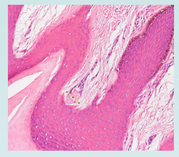

Fig 4 (b) Measurement taken of the Meissner Corpuscle

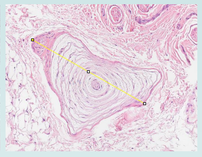

Fig 4 (c) Measurement taken of the Pacinian Corpuscle

Results

Mechanoreceptor Densities in the Macaque Foot

- MC density is significantly higher in toes 3 and 5 relative to the heel and the hallux (T1) (**Fig 5a)**
- PC density is significantly higher in toes 1 and 3 relative to the heel (**Fig 5b)**
- For both MC and PC, the densities in the toes overlap those found in parts of the hand (**Fig 6a & 6b**)

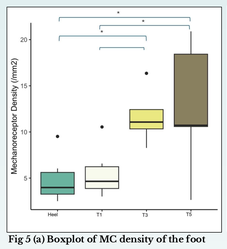

Fig 5 (a) Boxplot of MC density of the foot

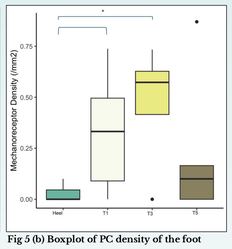

Fig 5 (b) Boxplot of PC density of the foot

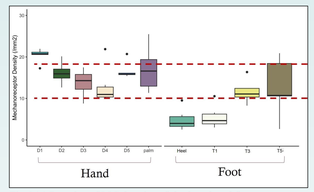

Fig 6 (a) Boxplot of MC density of the hand and foot

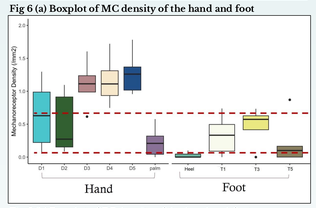

Fig 6 (b) Boxplot of PC density of the hand and foot

Innervation Densities in the Human Foot

- Innervation densities of FAI fibers (MCs) (**Fig 7a)** higher in toes vs. the heel and hallux, as in macaques
- Innervation densities of FAII fibers (PCs) (**Fig 7b)** are more consistent across the foot compared to macaques
- Human pedal innervation is much lower than manual innervation (**Fig 8a & 8b**)

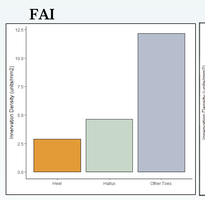

Fig 7 (a) Bar graph of Human Innervation densities of FAI fibers of the foot

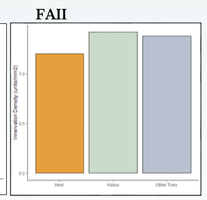

Fig 7 (b) Bar graph of Human Innervation densities of FAII fibers of the foot

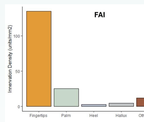

Fig 8 (a) Bar graph of Human Innervation densities of FAII fibers of the fingertips and foot

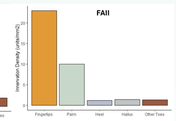

Fig 8 (b) Bar graph of Human Innervation densities of FAII fibers of the fingertips and foot

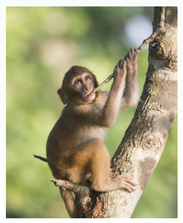

Fig 9 Juvenile Rhesus Macaque

Fig 10 Walking Human Figure

Summary

Similar MC and PC in the toes and hands of macaques may reflect need for sensitive touch during **pedal grasping and arboreal locomotion**

More consistent PC innervation in humans may reflect **changes due to bipedal locomotion**

Both humans and macaques show higher MC/FAI densities in toes, highlighting a **shared need to detect texture and object slippage regardless of locomotor style**

Conclusion

Baseline Mechanoreceptor Distribution:
- Provides foundational data on mechanoreceptor distribution in the feet of rhesus macaques.
- Contributes to understanding sensory adaptations in quadrupedal primates.

Fig 11: Geriatric Rhesus Macaque

Model for Somatosensory Aging:
- Characterizing standard mechanoreceptor distribution in healthy adult macaques is a prerequisite for using them as models for sensory impairments or somatosensory aging.

Relevance to Human Health:
- Age-related mechanoreceptor density changes in the feet are linked to reduced tactile sensitivity.
- Associated with increased risks of falls and balance-related injuries in humans.
- Understanding the distribution of mechanoreceptors in healthy rhesus macaques, which can also exhibit diabetic pathology, can enhance our knowledge of diabetic neuropathy in humans

Applications to Osteopathic Medicine

Improving Balance and Fall prevention in Aging
- Studies have highlighted how age-related declines in mechanoreceptor density can increase fall risks

Osteopathic Manipulative Treatment (OMT) could be used to enhance proprioception and improve balance in elderly patients, focusing on foot mechanics and sensory feedback pathways

Adaptations in Locomotor Functions:
- Insights into mechanoreceptor distributions in humans and macaques could guide osteopathic care for optimizing foot function in patients with impaired gait or locomotion such as post-injury rehabilitation

Somatosensory Feedback for Performance
- Shared higher density of Meissner corpuscles in toes across species suggests osteopathic interventions could target toes to improve sensory feedback for activities requiring precise footwork like athletics

Implications & Future Studies

How does this macaque pattern compare to mechanoreceptor densities in the human foot?

Future Research Directions:
- Investigate observed similarities and differences in mechanoreceptor distributions.
- Study the effects of aging on plantar mechanoreceptors in humans and macaques.

Fig 12: Rhesus Macaques Perched on a Tree Branch

Acknowledgements

Support for this project was provided by Midwestern University (CCV), Canada Research Chairs program (ADM), the New Frontiers Research Foundation NFRFE-2018-02159 (ADM and JPH), and the NIH (R01-MH096875, R01-MH118203, Office of Research Infrastructure Programs [ORIP] P40-OD012217).

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