

## Original Article

# The effect of running on functional MRI measures of hindfoot muscle activation due to ground reaction force

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Received December 19, 2016; Accepted January 25, 2017; Epub July 15, 2017; Published July 30, 2017

**Abstract:** This study explored the effect of ground reaction force on hindfoot muscle activation during jogging and recovery using functional magnetic resonance imaging (fMRI). Eight adult male volunteers (average age,  $36 \pm 8.3$  years; average height,  $1.73 \pm 0.03$  m; average weight,  $70 \pm 9.9$  kg) were asked to jog for 3000 meters on a treadmill at a velocity of 9 Km/hr and ground reaction force was measured using the Pedar<sup>®</sup> insole system. Muscle fMRI of each hindfoot muscle was performed immediately post exercise and compared to baseline imaging and imaging after 10, 20, 30 min, and 24 hours of rest. Significant positive correlation was observed between ground reaction force, expressed as Max force ( $r = 0.353$ ,  $P = 0.002$ ), peak pressure ( $r = 0.312$ ,  $P = 0.008$ ), force-time integral ( $r = 0.236$ ,  $P = 0.046$ ), and percent activated volume. T2 value was most pronounced in abductor digiti minimi (ADM) (lateral hindfoot territory). The most prominent activated volume was within posterior ADM. Greatest maximum force (33.17 N) occurred within flexor digitorum brevis (FDB) (central hindfoot territory). Ground reaction force resulted in metabolic changes on fMRI as reflected by percent activated volume within hindfoot muscles during jogging and this change was most pronounced immediately after exercise.

**Keywords:** Jogging, functional MRI, ground reaction force, running; Pedar<sup>®</sup> insole system

## Introduction

Jogging is a favorite pastime of the Taiwanese people and is increasing in popularity. However, running is associated with significant health issues related to force transmission from the ground (also known as ground reaction force or plantar pressure) [1-4]. An understanding of the relationship between metabolic changes within the plantar foot muscles and ground force transmission is essential for injury prevention, especially in the region of the central and lateral aspect of the hindfoot [2].

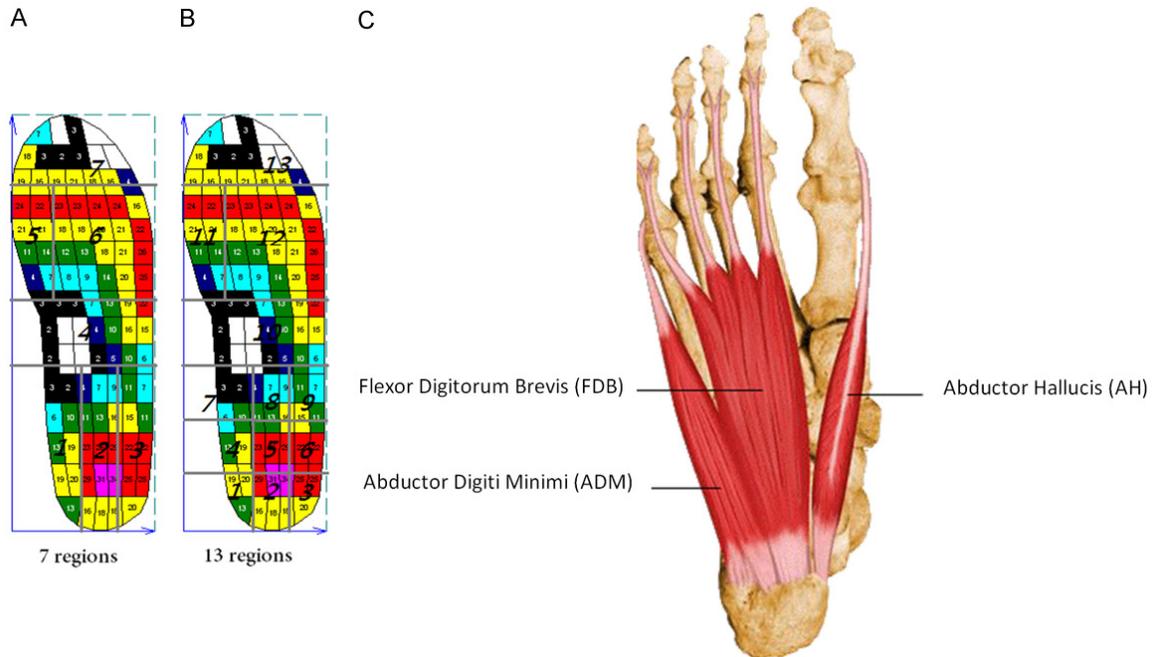
When running, since heel-strike is the first phase of stance [2, 5, 6], we evaluated the plantar foot muscles involved in heel-strike. These muscles include the abductor digiti minimi (ADM), flexor digitorum brevis (FDB), and abductor hallucis (AH) [7], corresponding to the lateral, central, and medial hindfoot, respec-

tively. The FDB acts as a plantar flexor of the foot to produce a propulsive “pushoff” through the joints of the lower limb [8, 9]. The ADM and AH act primarily to stabilize the lateral and medial arches of the foot.

Various foot pressure analysis studies have used surface EMG to detect foot pathology within these muscle groups during static standing [10-12]. However, static standing and running involve different movements. During running, variable ground reaction forces resulting from gravity and body segment accelerations are applied to the plantar surface of the foot and toes [8, 9]. To better evaluate the foot during active running, a more functional technique is needed such as functional MRI (fMRI).

Functional MRI (fMRI) is based primarily on the transverse relaxation time (T2 value) [13], since T2 is especially sensitive to metabolic and

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**Figure 1.** A. The foot is divided into seven regions: (1) medial rear foot, (2) central rear foot, (3) lateral rear foot, (4) mid foot, (5) first metatarsal head, (6) second to fifth metatarsal heads, (7) toes. B. The medial, central, and lateral hindfoot are further subdivided into another three regions for a total of 13 regions. C. Layer 1 (intrinsic muscles) includes abductors for the big toe (abductor hallucis, AH) and little toe (abductor digiti minimi, ADM). These act as additional “tie beams” for the arches of the foot. Centrally, the flexor digitorum brevis (FDB) flexes toes 2-5.

hemodynamic processes that accompany muscle activation. Muscle activation during fMRI is related to proton signal-intensity alterations related to the fluid shift of water in regions close to the activated location [14]. The increase in T2 has been used as an index of the intensity of muscle recruitment during various exercises [15]. Muscle fMRI signal changes have been shown to directly correlate with muscle contraction force level (motor units), EMG activity, and intensity of exercise [16]. Additional studies have shown that fMRI can be used to distinguish regional variations in activation during muscle contraction [16-18]. Changes in T2 also correlated well with integrated EMG activity for both concentric and eccentric contractions in biceps brachii [19].

Despite the development of fMRI techniques, few studies have investigated the correlation between MRI and external pressure exerted on the muscles involved in exercise. The relationship between ground reaction force and resulting metabolic changes within the heel is also unclear. In addition, whether ground force transmission can affect fMRI T2 values is unknown. This study was designed to explore

the effect of ground force transmission on heel muscle activity using fMRI during jogging and recovery. Our hypothesis concerned whether externally applied ground forces could generate metabolic changes within the hindfoot as measured using fMRI.

### Materials and methods

#### Participants

This study was approved by our Institutional Review Board and all participants gave their written informed consent prior to participate in the study.

Eight adult males (average age,  $36 \pm 8.3$  years; average height,  $1.73 \pm 0.03$  m; average weight,  $70 \pm 9.9$  kg) volunteered to participate in the study. None of the participants had any known neurologic or cardiovascular disorder. In order to prevent the biomechanical effect of ground force transmission, low and high arched feet were excluded. The participants were physically fit but had not engaged in specific resistance exercise involving the plantar flexor muscles prior to the experiment. The dominant foot (i.e.,

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the preferred leg for kicking a ball) was used during the experiment.

### *Ground reaction force measurement*

Each dominant foot was divided into seven regions (**Figure 1A**) including medial, central, and lateral hindfoot, midfoot, first metatarsal head, second to fifth metatarsal heads, and toes. Each activation level was considered non-uniformly distributed along each muscle length [16]. To delineate the ground force distribution in the hindfoot region, the medial, central, and lateral hindfoot were further subdivided into three additional regions for a total of 13 regions (**Figure 1B**).

The ground force distribution was measured using the Pedar<sup>®</sup> insole system (Novel gmbh, Munich, Germany) at 50 Hz. Throughout the experiment, all participants wore new running shoes which fit their feet and were of the same brand and category (i.e., Mizuno wave rider 14). The Pedar<sup>®</sup> insoles were placed between the socks and shoes and connected to the equipment. The insoles were 2.5 mm thick and contained a force sensing matrix of 99 capacitance sensors with a dynamic working range of 40-600 kPa. The insoles had a 10 mm spatial resolution corresponding to the slice thickness on MRI.

The software for the Pedar<sup>®</sup> system calculated 18 parameters. Our evaluation was carried out on four parameters including (1) maximum force (MaxF), defined as the maximum vertical ground force (N); (2) peak pressure (PP), defined as vertical ground force (N) divided by area (cm<sup>2</sup>) [20]; (3) pressure-time integral (PTI), defined as the integral of pressure with respect to time for each step; and (4) force-time integral (FTI) or the integral of force with respect to time. To compare MR images, plantar areas selected for pressure analyses included only the medial, central, and lateral hindfoot.

### *Exercise protocol*

A baseline MRI scan was performed pre-exercise. The participants then underwent a pre-trial adaptation phase involving jogging on the treadmill using the Pedar<sup>®</sup> footwear. The participants were then asked to jog for 3000 meters on the treadmill at a velocity of 2.5 m/s (9 Km/hr) in a comfortable position. The ground

reaction force on the heel was evaluated using the Pedar<sup>®</sup> insole system. The dominant foot was chosen because the muscle morphology of the dominant side is usually larger than the non dominant side. No stretches or cool down phase were allowed after the participants finished jogging. Because the jogging distance was consistent for every participant, the velocity of exercise was precisely recorded.

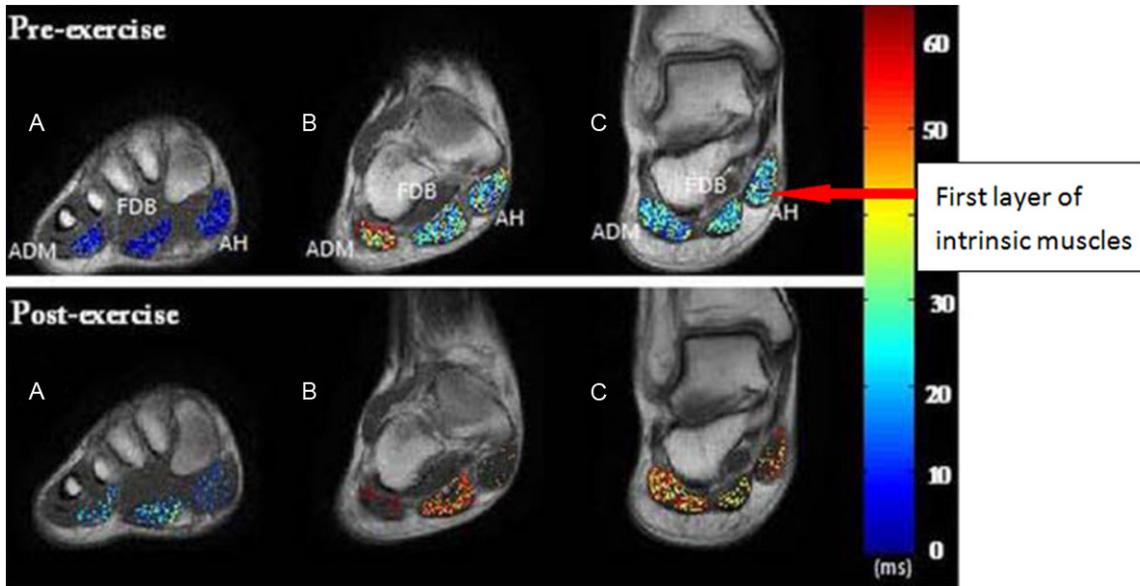
The exercise was performed outside the magnetic bore, and the participant was scanned immediately afterwards. The time interval between completion of the exercise and initiation of scanning was ~80 seconds. The participants were imaged at six time points, including before and immediately after the exercise and then every 10 min up to 30 min after the exercise. The final fMRI imaging was acquired 24 hours after exercise to evaluate the recovery phase after jogging.

### *Muscle functional MRI (fMRI)*

Muscle fMRI was performed using a 1.5 T MRI scanner (Achieva, Philips Medical Systems, the Netherlands). Each participant was positioned supine within the magnet.

A 2D multi-slice multi-echo spin echo (MESE) sequence (TR/TE1/TE10/FA: 786 ms/7.5 ms/75 ms/90°) was applied for the quantitative estimation of T2 values for ADM, FDB, and AH muscles corresponding to the lateral, central, and medial hindfoot, respectively, as shown in **Figure 1C**. The first TE was 7.5 ms and 9 spin echoes were sampled, thereafter, every 7.5 ms for a total examination time of 18 sec. Two signal averages and a SENSE factor of 1.6 were used.

Images were collected from the posterior calcaneal tuberosity to the shaft of metatarsals to obtain the muscle cross-sectional area. Thirteen continuous 10-mm-thick axial slices covered the entire region of interest (ROI) [21] and were acquired with a 0-mm gap between slices. The field of view (FOV) was 110 × 103 mm, and the data were collected using a 124 × 191 matrix. The shorter axis (at approximately the seventh of the 13 slices) was parallel to tibiotalar joint (superior facet) in the coronal plane, and the center of the FOV was placed 20 mm below the tarsal sinus. The shorter axis of each



**Figure 2.** Representative  $T_2$  values within foot muscles in the axial plane located within the distal (A), middle (B), and proximal (C) foot from a single participant before and after exercise. The color coded muscles (red arrow) indicates the first layer of intrinsic muscles.

slice was prescribed perpendicular to the axis connecting the medial side of the cuboid and posterior calcaneal tuberosity of foot in the axial plane.

#### Imaging analysis

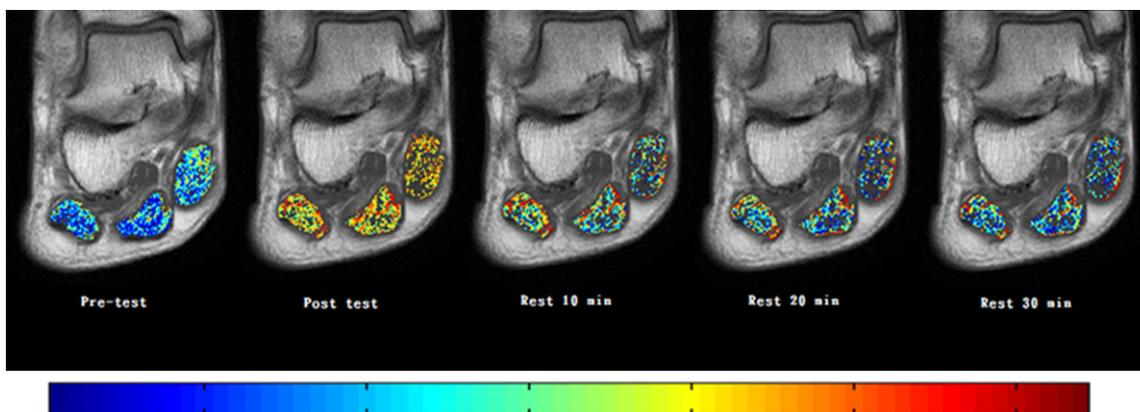
All MR images were transferred to a personal computer off-line.  $T_2$  values were subsequently calculated by fitting signal intensities for varying TEs to a monoexponential decay model using the Marquardt-Levenberg algorithm [22].

$T_2$  images obtained from six time points were analyzed to investigate the time course of change in  $T_2$  values. Representative  $T_2$  values in the axial plane from a single participant before and after exercise are shown in **Figure 2**. The FDB, ADM, and AH are considered the first of four layers of intrinsic muscles of the sole, as shown in **Figure 2**.

We established ROIs for the ADM, FDB, and AH muscles by manually tracing around the image on a slice-by-slice basis for each muscle group. Care was taken to exclude intramuscular fat, aponeurosis, and vascular structures from the traced regions. The  $T_2$  value of each voxel within an ROI was calculated, and the mean and SD of the  $T_2$  value for each individual muscle were determined.

The method of Kinugasa et al. [14, 16, 18, 23] was used to define the active muscle region within each individual muscle after exercise. In brief, pixels showing  $T_2$  values greater than the mean +1 SD of the ROI in the before-exercise image and less than the mean +1 SD in the image immediately after exercise were identified.  $T_2$  values within the range defined by the two thresholds were considered to be the active muscle region after jogging. Additionally,  $T_2$  values that fell within the accepted range in the before-exercise images were divided into five categories. Because the exercise-induced change in  $T_2$  was related to the force level [13, 19], these categories were considered indices of the activation level of the exercised muscle fibers. Activation levels were defined from lowest (level 1) to highest (level 5), and coded by color from blue (lowest) to red (highest activation level) (**Figure 3**). The activated volume from each color map was then determined using the active muscle region multiplied by the 10 mm slice thickness, over the entire ROI. The activated volume was then expressed relative to the total anatomical volume as a percent (i.e., the percent activated volume) for each muscle at each of the five levels.

Furthermore, active muscle regions defined by the two thresholds were copied to the corresponding regions as a reference to acquire  $T_2$



**Figure 3.** Evolution of activated muscle over time from pre-exercise, through immediate post exercise, to rest. The muscle activation is coded by color from red (highest activation level) to blue (lowest activation level).

values at 10, 20 and 30 min time points, and to also acquire temporal changes and spatial changes in T2 values for the identical regions of individual muscles.

#### Statistical analysis

The ground reaction force (MaxF), PP, FTI, PTI, total muscle volume, changes in T2, and activated volume for three hindfoot areas (anterior, middle, posterior) and three muscles (ADM, FDB, AH) were expressed as medians with inter-quartile ranges (**Tables 1** and **2**). The non-parametric Friedman test was performed to detect whether differences existed between the various areas or muscles. If the Friedman test was significant, the non-parametric Wilcoxon signed ranks test was performed for post-hoc comparisons.

To investigate the correlations between ground reaction force, peak pressure, FTI, PTI, and MRI results (total muscle volume, T2 change and activated volume), the Pearson correlation coefficients ( $r$ ) were calculated. The effect of individual muscles (ADM, FDB, and AH muscles) on the activated volume for five activation levels was determined by the linear mixed model with stratification of area (anterior, middle, posterior). The effect of individual muscles (ADM, FDB, and AH muscles) and time course on T2 were also evaluated by the linear mixed model with stratification of area (anterior, middle, posterior). In addition, the paired t-test was performed to compare the T2 values between two time points for a specified hindfoot or between two hind feet for a specified time point. Statistical analyses were assessed by using SPSS soft-

ware version 15.0 (SPSS Inc., Chicago, IL, US). A two-tailed  $P$ -value  $< 0.05$  was considered significant.

#### Results

##### *Measurement of ground reaction force on hindfoot muscles using the Pedar<sup>®</sup> insole maximum force (MaxF)*

In the anterior hindfoot, MaxF was exerted on FDB (15.20 N) and was significantly higher than the force exerted on AH (7.75 N). In the middle hindfoot area, the MaxF was exerted on FDB (33.17 N) and was significantly higher compared with either ADM (29.27 N) or AH (22.72 N). In the posterior hindfoot area, the MaxF was exerted on FDB (30.68 N) and was significantly higher compared with either ADM (26.28 N) or AH (14.51 N).

Within the ADM muscle itself, the MaxF exerted on its middle area (29.27 N) was significantly higher than the force exerted on its anterior (11.98 N). In the FDB muscle, the MaxF on either middle (33.17 N) or posterior (30.68 N) areas was significantly higher than the force exerted on the anterior area (15.2 N). In the AH muscle, the MaxF on either middle (22.72 N) or posterior (14.51 N) areas was significantly higher than the force exerted on the anterior area (7.75 N) (**Table 1**).

##### *Peak pressure (PP)*

In the anterior and posterior areas, the PP within AH was significantly lower than the PP within either ADM or FDB (anterior: 6.89 vs. 10.07 or

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**Table 1.** Ground reaction force for the different hindfoot muscles and regions

	Area	ADM	FDB	AH	P-value*
MaxF (N)	Anterior	11.98 (9.27, 18.91)	15.20 (12.02, 16.59)	7.75 (5.89, 9.61) <sup>†,‡</sup>	0.008
	Middle	29.27 (24.19, 32.13) <sup>a</sup>	33.17 (30.43, 39.03) <sup>†,a</sup>	22.72 (19.09, 23.82) <sup>‡,a</sup>	< 0.001
	Posterior	26.28 (13.26, 33.57)	30.68 (20.88, 44.32) <sup>†,a</sup>	14.51 (13.30, 20.72) <sup>‡,a</sup>	0.001
	P-value*	0.018	0.008	< 0.001	
PP (N/cm <sup>2</sup> )	Anterior	10.07 (7.38, 12.49)	10.16 (7.80, 11.10)	6.89 (5.43, 8.42) <sup>†,‡</sup>	0.001
	Middle	17.88 (16.22, 21.50) <sup>a</sup>	17.62 (16.46, 21.51) <sup>a</sup>	16.57 (14.96, 17.87) <sup>a</sup>	0.086
	Posterior	17.92 (11.20, 23.97) <sup>a</sup>	16.42 (11.98, 24.86) <sup>a</sup>	11.51 (9.76, 14.97) <sup>†,‡,a,b</sup>	0.002
	P-value*	0.008	0.008	0.001	
FTI (N*s)	Anterior	0.98 (0.65, 1.65)	1.19 (0.89, 1.29)	0.48 (0.36, 0.81) <sup>†,‡</sup>	0.008
	Middle	2.06 (1.53, 2.83) <sup>a</sup>	2.48 (2.24, 3.54) <sup>a</sup>	1.67 (1.28, 1.95) <sup>a</sup>	< 0.001
	Posterior	1.50 (0.73, 2.08) <sup>b</sup>	2.01 (1.22, 3.14)	0.81 (0.73, 1.45) <sup>†,‡</sup>	0.001
	P-value*	0.001	0.018	0.007	
PTI (N/cm <sup>2</sup> *s)	Anterior	0.80 (0.58, 1.17)	0.84 (0.54, 0.95)	0.47 (0.35, 0.71) <sup>‡</sup>	0.006
	Middle	1.34 (1.14, 2.02) <sup>a</sup>	1.32 (1.22, 2.02)	1.33 (1.14, 1.59) <sup>a</sup>	0.086
	Posterior	1.16 (0.72, 1.67) <sup>b</sup>	1.11 (0.74, 1.76) <sup>†</sup>	0.68 (0.59, 1.06) <sup>‡,b</sup>	0.002
	P-value*	0.001	0.079	0.001	

Abbreviations: MaxF, maximum force; PP, peak pressure; PTI, pressure-time integral, FTI: force-time integral; ADM, abductor digiti minimi; FDB, flexor digitorum brevis; AH, abductor hallucis. Data are expressed as medians with inter-quartile ranges.

\*The *p*-values were performed by the Friedman test. The results of post-hoc tests (Wilcoxon signed ranks tests) are represented by the following markers: <sup>†</sup>indicates a significant difference compared to ADM; <sup>‡</sup>indicates a significant difference compared to FDB; <sup>a</sup>indicates a significant difference compared to anterior; <sup>b</sup>indicates a significant difference compared to middle.

10.16 N/cm<sup>2</sup>; posterior: 11.51 vs. 17.92 or 16.42 N/cm<sup>2</sup>). Within each muscle, the PP in middle and posterior areas was significantly higher than the PP in the anterior area (ADM: 17.88 and 17.92 vs. 10.07 N/cm<sup>2</sup> respectively; FDB: 17.62 and 16.42 vs. 10.16 N/cm<sup>2</sup>, respectively; AH: 16.57 and 11.51 vs. 6.89 N/cm<sup>2</sup>, respectively) (**Table 1**).

### Force-time integral (FTI)

In the anterior and posterior areas, the FTI within AH was significantly lower than the FTI within either ADM or FDB (anterior: 0.48 vs. 0.98 or 1.19 N\*s; posterior: 0.81 vs. 1.50 or 2.01 N\*s). The FTI within ADM was significantly higher in middle area compared to anterior and posterior areas (2.06 vs. 0.98 vs. 1.50 N\*s, respectively). The FTIs within FDB and AH were significantly higher in the middle area compared to the anterior area (FDB: 2.48 vs. 1.19 N\*s, respectively; AH: 1.67 vs. 0.48 N\*s, respectively) (**Table 1**).

### Pressure-time integral (PTI)

In the anterior and posterior areas, the PTI within AH was significantly lower than the PTI within FDB (anterior: 0.47 vs. 0.84 N/cm<sup>2</sup>\*s, respec-

tively; posterior: 0.68 vs. 1.11 N/cm<sup>2</sup>\*s, respectively). The PTI of ADM and AH were significantly higher in the middle area compared to either anterior or posterior areas (ADM: 1.34 vs. 0.80 or 1.16 N/cm<sup>2</sup>\*s, respectively; AH: 1.33 vs. 0.47 or 0.68 N/cm<sup>2</sup>\*s, respectively) (**Table 1**).

### Total muscle volume, T2 change and percent activated volume for various hindfoot areas

There were no significant differences in total muscle volume between types of muscles in the anterior area (*P* = 0.079) (**Table 2**). Muscle volumes within FDB and AH were higher than that within ADM in the middle area of the hind-foot (2140.0 and 2525.0 vs. 1334.5 mm<sup>3</sup> for FDB and AH, respectively). In the posterior area, muscle volume was lower within FDB than ADM or AH (1190.5 vs. 1805.5 mm<sup>3</sup> within FDB and 1849.0 mm<sup>3</sup> within AH). Significant differences in total muscle volumes within ADM and FDB were also found (*P* = 0.018 for ADM and 0.002 for FDB). Results showed higher muscle volumes in the posterior area of ADM as compared with the middle area (1805.5 vs. 1334.5 mm<sup>3</sup>), whereas muscle volume in the posterior area of FDB was the lowest as compared with other two areas (1190.5 vs. 1490.0 for anterior

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**Table 2.** T2 change and percent activated volume for the different hindfoot muscles and regions

		ADM	FDB	AH	P-value*
Total muscle volume (mm <sup>3</sup> )	Anterior	1564.5 (1354.5, 2201.5)	1490.0 (1408.5, 1721.5)	1831.0 (1560.5, 2011.5)	0.079
	Middle	1334.5 (1043.0, 1459.0)	2140.0 (1773.5, 2223.5) <sup>†,a</sup>	2525.0 (1945.0, 3118.5) <sup>†</sup>	0.005
	Posterior	1805.5 (1512.0, 2014.0) <sup>b</sup>	1190.5 (827.0, 1439.5) <sup>†,a,b</sup>	1849.0 (1312.5, 2429.5) <sup>†</sup>	0.008
	P-value*	0.018	0.002	0.149	
T2 change immediately after exercise (%)	Anterior	16.54 (13.17, 22.72)	15.95 (14.55, 20.12)	14.16 (12.95, 18.40)	0.120
	Middle	18.54 (17.97, 24.84)	17.99 (14.54, 18.67)	16.87 (13.33, 19.17) <sup>†</sup>	0.018
	Posterior	17.32 (16.00, 23.69)	13.46 (10.38, 17.94)	13.23 (11.58, 16.31) <sup>†,b</sup>	0.005
	P-value*	0.531	0.285	0.010	
Activated volume (%)	Anterior	22.24 (13.06, 29.74)	19.57 (11.23, 25.51)	18.32 (12.55, 22.54)	0.236
	Middle	26.58 (22.34, 30.28)	27.53 (24.40, 43.69)	17.87 (14.89, 27.09) <sup>†</sup>	0.005
	Posterior	33.24 (25.03, 41.07) <sup>a</sup>	29.83 (23.90, 43.71)	23.47 (14.61, 38.54)	0.531
	P-value*	0.018	0.120	0.079	

Abbreviations: ADM, abductor digiti minimi; FDB, flexor digitorum brevis; AH, abductor hallucis. Data are expressed as medians with inter-quartile ranges. \*The p-values were performed by the Friedman test for three related samples, and the Wilcoxon signed ranks tests were performed for post-hoc comparisons when the Friedman test was statistically significant. The results of post-hoc testing are represented by the following markers: †indicates a significant difference compared to ADM; ‡indicates a significant difference compared to FDB; §indicates a significant difference compared to anterior area; ¶indicates a significant difference compared to middle area.

**Table 3.** Correlation between ground reaction force vs. T2 change and activated volume

	MaxF		Peak pressure		FTI		PTI	
	r	P-value	r	P-value	r	P-value	r	P-value
Total muscle volume (mm <sup>3</sup> )	0.038	0.750	0.092	0.441	0.118	0.324	0.174	0.144
T2 change immediately after exercise (%)	0.141	0.237	0.158	0.184	0.144	0.226	0.170	0.154
Activated volume (%)	0.353	0.002*	0.312	0.008*	0.236	0.046*	0.181	0.129

Abbreviations: r, Pearson correlation coefficient; MaxF, maximum force; PTI, pressure-time integral; FTI, force-time integral. \*P < 0.05 indicates a significant correlation.

and 2140.0 mm<sup>3</sup> for middle areas, respectively). In the middle and posterior areas of the hindfoot, the T2 change (expressed as percent activated volume) within AH was significantly lower than the T2 change within ADM (middle: 16.87% vs. 18.54%, respectively; posterior: 13.23% vs. 17.32%, respectively) Within AH, posterior T2 change was significantly lower than middle T2 change (13.23% vs. 16.87%, respectively) (**Table 2**). In the middle area, the activated volume within AH was significantly lower than the activated volume within FDB (17.87% vs. 27.53%, respectively). Within ADM, posterior activated volume was significantly higher than anterior activated volume (33.24 vs. 22.24%, respectively) (**Table 2**).

### Correlations between ground reaction force and MRI results

Significant positive correlations were observed between MaxF (r = 0.353, P = 0.002), PP (r = 0.312, P = 0.008), and FTI (r = 0.236, P = 0.046) versus activated volume (**Table 3**), but

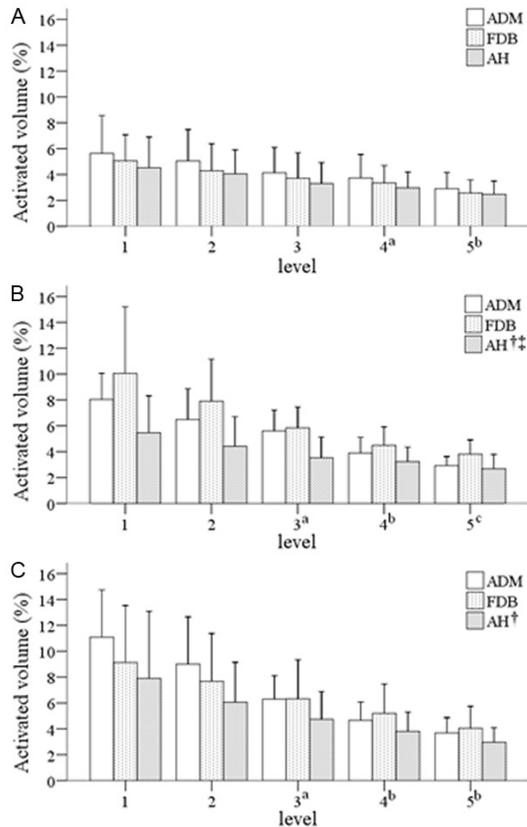
no significant correlation was observed between the ground reaction force and T2 change as well as total muscle volume. Furthermore, T2 change immediately after exercise positively correlated with total muscle volume (r = 0.487, P < 0.001) and activated volume (r = 0.511, P < 0.001). Activated volume was not related to total muscle volume (r = 0.137, P = 0.252) (data not shown).

### Effects of activation level on percent activated volume within hindfoot muscles

At the exercise load used in this study, the percent activated volumes decreased as the activation level increased, regardless of the area of the hindfoot involved [i.e., anterior, middle, or posterior areas (shown as A, B, and C, respectively, in **Figure 4**)].

In the anterior area of the hindfoot (**Figure 4A**), the activated volume at level 4 was significantly lower than at level 1 (with estimated mean difference of -1.73%, P = 0.001), and the activat-

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**Figure 4.** Activated volumes within the ADM, FDB, and AH muscles for five activation levels. (A) Anterior area (B) Middle area (C) Posterior area. Bars represent the means  $\pm$  SD for all subjects. †indicates a significant difference compared to ADM while controlling for activation level, ††indicates a significant difference compared to FDB while controlling for activation level, †††indicates a significant difference compared to level 1 while controlling for hindfoot muscle, ††††indicates significant differences compared to level 1 and level 2 while controlling for hindfoot muscle, †††††indicates significant differences compared to level 1, level 2, and level 3 while controlling for hindfoot muscle.

ed volume at level 5 was significantly lower than at levels 1 and 2 (with estimated mean differences of -2.43% and -1.82%,  $P \leq 0.001$ ).

In middle and posterior areas of the hindfoot (Figure 4B and 4C, respectively), the activated volume at level 3 was significantly lower than at level 1 (with estimated mean differences of -2.86% and -3.59%,  $P < 0.001$ ), and the activated volumes of levels 4 and 5 were significantly lower than at levels 1 and 2 (middle area: estimated mean differences for level 4 compared to levels 1 and 2 of -3.98% and -2.4%, respectively; estimated mean differences for

level 5 compared to level 1 and 2 of -4.72% and -3.13%, respectively; posterior area: estimated mean differences for level 4 compared to levels 1 and 2 of -4.82% and -3.03%; estimated mean differences for level 5 compared to levels 1 and 2 of -5.81% and -4.02%, respectively; all  $P$ -values  $< 0.001$ ) (Figure 4B and 4C).

Furthermore, while controlling for activation level, ADM and FDB had greater activated volumes than AH in the middle area (Figure 4B); and ADM had a greater activated volumes than AH in the posterior area (Figure 4C). At the anterior area, no significant differences in activated volume were observed among ADM, FDB, and AH (Figure 4A).

### Correlation between hindfoot muscles and T2 values

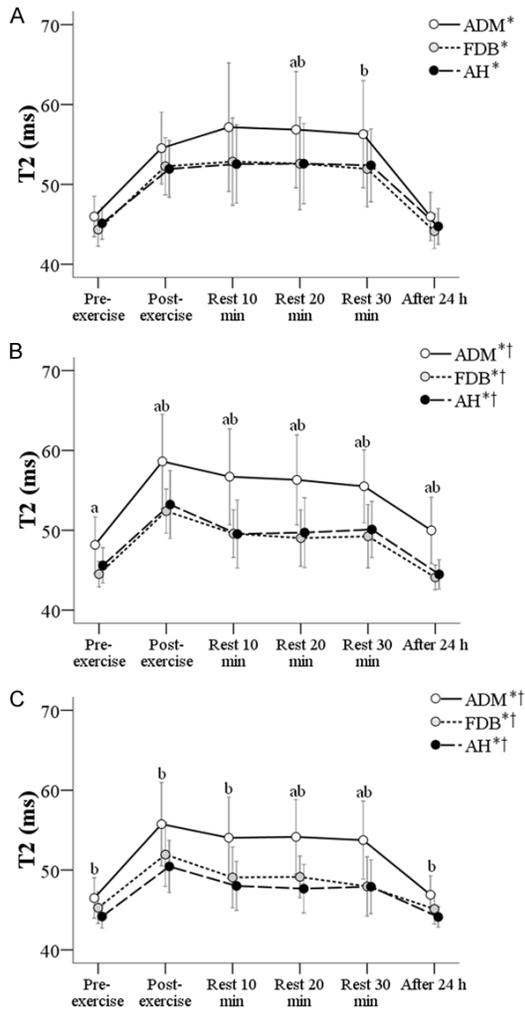
Regardless of area (i.e., anterior, middle, or posterior), the T2 values within ADM were significantly higher than the T2 values within FDB or AH while controlling for time in the linear mixed models, with an estimated difference in means of 3.11 ms ( $P = 0.001$ ) and 2.91 ms ( $P = 0.002$ ) for FDB and AH, respectively, at the anterior area; of 6.08 ms and 5.44 ms (both  $P < 0.001$ ) for FDB and AH, respectively at middle area; and of 3.76 ms and 4.79 ms (both  $P < 0.001$ ) for FDB and AH, respectively, at posterior area.

Regardless of area (i.e., anterior, middle, or posterior), all three hindfoot muscles showed significantly higher T2 levels immediately post-exercise and after 10, 20, 30 mins of rest compared to pre-exercise and 24 hours after exercise (all  $P$ -values  $< 0.05$ ; Figure 5). Furthermore, in the middle and posterior areas, all three hindfoot muscles had T2 levels immediately post-exercise which were significantly higher compared to 10, 20, 30 mins of rest after exercise (all  $P$ -values  $< 0.05$ ; Figure 5).

### Discussion

This study used the Pedar<sup>®</sup> insole system to investigate how ground reaction force during jogging affected the T2 value measured during fMRI. A significant positive correlation was observed between ground reaction force (expressed as MaxF), and percent activated volume. But no significant correlation was observed between the ground reaction force and

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**Figure 5.** Time course of T2 change within ADM, FDB, and AH muscles. (A) Anterior area (B) Middle area (C) Posterior area. All values are expressed as means  $\pm$  SD. \* indicates significant differences of post-exercise, rest for 10, 20, 30 minutes vs. pre-exercise and after 24 hours; † indicates significant differences of rest for 10, 20, 30 minutes vs. post-exercise. ‡ indicates a significant difference between ADM and FDB. †‡ indicates a significant difference between ADM and AH.

T2 change or total muscle volume, Using the Pedar<sup>®</sup> insole, the MaxF was greatest in the central hindfoot (FDB territory) regardless of the area (anterior, middle, posterior) of the hindfoot studied. This study also showed that, at the exercise load used, the percent activated volumes decreased as the activation level increased, regardless of the area of the hindfoot involved. This result suggested that the metabolic change induced by the ground reaction force was most pronounced immediately after exercise. The T2 value was also shown to plateau 10 mins after exercise, and to recover

to pre-exercise levels after 24 hours, and the effect was most pronounced in ADM, regardless of the area of the hindfoot studied.

Quantitative T2 fMRI is a powerful tool that can monitor muscle activation and enhance the study of biomechanics and muscle physiology after exercise. Muscle fMRI has been frequently used to examine the intensity of muscle activation. The T2 increase measured by MRI methods has been used in many studies as an index of the intensity of muscle recruitment during various exercises [15]. Moreover, Kinugasa and Akima found a significant correlation between T2 values and integrated EMG activity in the medial gastrocnemius and soleus, but not in lateral gastrocnemius [23]. These results have important practical implications for the use of muscle T2 as an index of muscle activity during exercise.

Muscle fMRI has been frequently used to examine the intensity and pattern of muscle activation. Exercise-induced shifts in T2 values have correlated with integrated electromyography activity [18, 19]. Kinugasa et al. indicated that individual triceps surae muscles play different functional roles during contraction [18]. To the best of our knowledge, however, no other study has shown a correlation between the MaxF and metabolic changes on fMRI, as reflected by percent activated volume within ADM, FDB, and AH muscles during muscle activation. Therefore, MaxF may represent a new index of hindfoot muscle activation, in addition to EMG.

### Percent activated volume within ADM, FDB, and AH muscles

Our study also investigated activation levels within ADM, FDB, and AH muscles and examined the recovery of muscle T2 values after jogging. Our results showed that FDB contained a larger percentage of activated volume compared with either AH or ADM. From an anatomical and physiological point of view, the faster contraction times seen in the FDB can be explained by either their architecture and/or their underlying fiber type distribution [24-26].

Similarly, Tosovic et al. also found that the average whole muscle contraction time ( $T_c$ ) of FDB was significantly shorter (faster) ( $T_c = 58$  ms) than all other foot muscles investigated (ADM  $T_c = 72$  ms, extensor digitorum brevis (EDB)  $T_c = 72$  ms, and AH  $T_c = 69$  ms) [27]. According to

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Tosovic et al., faster FDB contraction time could be explained by the direct agonist toe-flexion role the FDB plays during explosive 'push-off' during running [27].

These results suggest that the architecture and contraction time of FDB reflect its unique direct contribution (through toe flexion) to postural stability and the rapid development of ground reaction forces during forceful activities such as running and jumping [27]. FDB becomes active exclusively between 40% and 65% of the gait cycle, corresponding to the terminal stance/pre-swing phases of the cycle, in which the plantar flexors of the foot act concentrically in producing the propulsive "push-off" through the joints of the lower limb [8, 9].

We also found that for each muscle, the percent activated volume at a low level of activation (level 1) was larger than that at a high level of activation (level 5). Apparently, the jogging exercise used in the present study was primarily associated with a low intensity level of hindfoot muscle activation [16].

### *T2 recovery of muscle activation over time*

The recovery of ADM, FDB, and AH was highest at 10 minutes following cessation of exercise and then plateaued and finally dropped to initial levels at 24 hours after exercise. Our findings demonstrated important differences regarding the time course of recovery compared with the results of Reid et al. [15]. Their recovery curve appeared as a gradually decreasing smooth curve, however our recovery curve was very different. The activity-induced increase in T2 intensity was detectable after exercise and rose to an intensity-dependent level within a few minutes. Our recovery information suggests that it is quite possible to acquire functional images after performing a task outside the scanner room. Reid et al. [15] also found that full T2 recovery could require as long as 30-40 minutes. There is a good correlation between the T2 increase and the extent of phosphocreatine hydrolysis and muscle acidification immediately after exercise in human muscle, although the T2 change recovers more slowly after exercise compared with these metabolic changes [15]. Meyer et al. reported that recovery after exercise takes 20 min or more [13]. However, our data suggest that recovery

of muscle activity begins 10 minutes after running and full recovery occurs 24 hours later.

Our study had several limitations including its small sample size and the use of only male participants in the study. In addition, our evaluation was limited to just the hindfoot. Therefore, future studies involving the entire foot with larger patient cohorts of both genders are needed to confirm our findings. In addition, jogging on a treadmill is very different from participating in a road race, and our results cannot be extrapolated to a race. Finally, as all of the fMRI measures were obtained after running, no claims can be made about the role of a given muscle during running.

In conclusion, this study represents the first application of the Pedar<sup>®</sup> insole system towards an understanding of the relationship between ground reaction force (expressed as MaxF) and T2 changes within hindfoot muscles using fMRI. MaxF derived from this study could represent a new index of hindfoot muscle activation since ground reaction force resulted in metabolic changes on fMRI that were reflected by percent activated volume within ADM, FDB, and AH muscles during jogging.

Understanding the relationship between metabolic changes and ground force transmission in the foot are also important for devising methods of injury prevention and treatment, including improvements in shoe design based on reducing pressure using sole cushions. Since ground reaction force was greatest within the central hindfoot (FDB territory) regardless of the area (anterior, middle, posterior) of the hindfoot studied, such future design work should focus primarily on the central hindfoot, based on the results of this study.

### **Acknowledgements**

Both the MRI scanner and Dr. Huan-Chu Lo's research were funded by Tao-Yuan General Hospital Grant 10326 and TSGHIRB No: TY-102-05.

### **Disclosure of conflict of interest**

None.

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