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A Novel Approach to Evaluate Brain Activation for Lower Extremity Motor Control

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Abstract

Background and Purpose: The purpose of this study was to assess the consistency of a novel MR safe lower extremity motor control neuroimaging paradigm to elicit reliable sensorimotor region brain activity.

Method: Participants completed multiple sets of unilateral leg presses combining ankle, knee, and hip extension and flexion movements against resistance at a pace of 1.2 Hz while lying supine in a 3T MRI scanner. Regions of Interest (ROI) consisted of regions primarily involved in lower extremity motor control (right and left primary motor cortex, primary somatosensory cortex, pre-motor cortex, secondary somatosensory cortex, basal ganglia, and the cerebellum).

Results: The group analysis based on mixed effects paired samples *t*-test revealed no differences for brain activity between sessions ($p>0.05$). Intraclass correlation coefficients in the sensorimotor regions were good to excellent for average percent signal change (0.621 to 0.918) and Z-score (0.697 to 0.883), with the exception of the left secondary somatosensory cortex percent signal change (0.165).

Conclusions: These results indicate that a loaded lower extremity force production and attenuation task that simulates the range of motion of squatting, stepping, and landing from a jump

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is reliable for longitudinal neuroimaging applications and support the use of this paradigm in further studies examining therapeutic interventions and changes in dynamic lower extremity motor function.

Keywords

Reliability; Neuroimaging; Knee; Leg press

Introduction

Coordinated locomotor activities such as jumping, climbing stairs, and running are complex motor skills that require effective coordination between the central and peripheral nervous system. While there is extensive knowledge pertaining to the physiologic,[1–3] biomechanical,[4–7] and neuromuscular[8,9] components of lower extremity dynamic human movement, less is understood regarding the underlying neural activity driving lower extremity complex action. Recent innovations with electroencephalography (EEG) have allowed neural recording during dynamic multi-joint lower extremity coordinated movements.[10–13] However, EEG only measures surface cortical activity and lower extremity motor control has an extensive sub-cortical and cerebellar component. Other modalities do allow quantification of cortical function during dynamic tasks such as single-photon-emission-computed-tomography (SPECT),[14,15] positron emission tomography (PET)[16] and functional near-infrared spectroscopy (fNIRS).[17–19] On the other hand, these modalities are limited in their spatial resolution and/or only allow for measuring a minimal degree of lower extremity movement.

Advances in neuroimaging have made it possible to obtain highly accurate spatial images of neural functioning using fMRI.[20–25] However, fMRI requires participants to stay in the supine position with their head still for prolonged periods of time. This can be technically challenging in acquiring accurate neural readings, simultaneous with lower limb multi-joint movements.[26] As many of the primary hip and knee joint muscles originate from the pelvis, such as hip flexors, gluteals, hamstrings and quadriceps, any lower limb movement proximal to the ankle are predisposed to induce pelvic and trunk translation and head motion artifacts. This has resulted in considerable concern pertaining to the impact of head motion as a confounding factor during motor task fMRI data acquisition[5,27] with subsequent image-processing schemes developed to minimize head motion artifacts.[28–31] Nonetheless, the image re-alignment processes cannot fully eliminate excessive head motion, nor account for task-correlated motion.[32] As a result, researchers have opted towards a solution that includes constraints and supports of the lower limbs and pelvis, allowing for freedom of movement while keeping the head stable.[26]

A number of studies have developed novel MRI-safe devices permitting participants to execute locomotive-like functions while in the MRI machine.[33,34] An early attempt utilized ankle dorsiflexion in order to examine cortical adaptations for walking therapies[35] as ankle dorsiflexion is a foundational component for normal gait. Expansions on this work have utilized an isometric leg press device allowing for isometric (muscle contraction without movement) ankle, knee, and hip extension.[26] Increased activation in the sensorimotor cortex, the dorsolateral premotor cortex, the supplementary motor area, and in the secondary

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somatosensory cortex was observed on two separate testing sessions with medium to high reliability demonstrating the efficacy of such apparatus for measuring cortical function associated with ankle and knee extension contractions.[26] However, the actions were isometric (no movement) and at very low force levels. A few studies have evaluated more functional knee flexion and extension movements within an MRI scanner,[36–38] and while these studies allowed for knee movement, they were not against external resistance nor allowed hip motion. More complex pedaling devices have been used to simulate the rhythmic alterations of lower limb flexion and extension during walking,[34] including an MRI safe stepping device termed the Magnetic Resonance Compatible Stepper (MARCOS) which simulates participants' movements and physical forces as if walking.[39] MARCOS was successfully used with fMRI to determine differences in neural activation between active versus passive lower-limb, bilateral, multi-joint movements,[24] with active tasks exhibiting greater sensorimotor region activation relative to passive tasks. Greater sensorimotor activation for active tasks were consistent with prior reports demonstrating increased activation during locomotion,[34,40] and have provided valuable insight into the neural mechanisms underlying human movement.

While prior studies have helped further scientific understanding of lower limb multi-joint motor movements, there is still a need for devices that simulate other locomotive processes beyond simple single joint movements or simulated gait. For instance, the biomechanics employed during jumping,[41–43] squatting,[25,44] and running[45,46] elicit hip flexion and extension when an individual's lower extremity is in contact with the ground (i.e., closed-kinetic chain [CKC] exercise) across the entire stretch-shortening cycle. CKC movements are also typically 'loaded' in which the knee and hip extension movements are against resistance (typically bodyweight). Functional loaded movements are common behavioral outcome measures of exercise,[47,48] injury prevention,[49,50] and motor learning interventions,[51,52] and are also vital for sport or recreational activities that require proper mechanics to avoid injury.[53,54] A neuroimaging paradigm that simulates functional loaded movement could guide novel treatment for musculoskeletal disorders that exhibit both motor control and neural activity alterations (e.g., anterior cruciate ligament [ACL] injury).[36,55] However, no reliable fMRI paradigm has been developed that specifically targets these loaded multi-joint movements. The purpose of the present study was to present a novel method to assay brain activation during coordinated lower extremity movement under load and to evaluate the consistency of the neuroimaging paradigm to induce sensorimotor region activity.

Methods

Participants

Thirteen healthy female participants (mean age = 16.23 +/− 0.72 yrs; mean height = 163.85 +/− 4.67 cm; mean weight = 59.56 +/− 8.70 kg) volunteered for this study. Participants were all of similar fitness and participation levels, were members of the same high school soccer team, and did not engage in any specific or novel training beyond school sponsored athletics. All participants (and parent or legal guardian if under 18) signed an informed consent/assent and completed an MRI screening form. Volunteers participated in the full protocol on two

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separate testing sessions separated by 7.10 (+/− 0.98) weeks. The study was approved by the institutional review board at Cincinnati Children’s Hospital Medical center.

Instrumentation

The leg-press testing apparatus was custom built and comprised of two pedals that ran on tracks. This design permitted the participant to complete repetitive combined ankle, knee and hip extension and flexion movements that mimic the loading pattern for landing. The participant laid on the MR scanner table in the supine position with earplugs for auditory protection. The participants’ head was positioned in the head coil such that the top of the headphones abutted the top of the coil (reducing potential inferior to superior head translation during imaging). Small foam padding was put on the sides of the headphones in order to fill any gaps between the participants’ head and the inner head coil to further secure the head in place. The feet of the participant were strapped into the pedals with their legs in full extension. The pedals moved with flexion and extension of the hip and knee. Rubber resistance bands were put around the pedals and connected to the unit to provide resistance when the participant extended their lower extremity.

In order to minimize head movement from forces exerted at the knee and hip during the unilateral simulated landing movement, multiple strategies were engaged. Fluidized positioners (Sundance Solutions, White Plains, NY) were placed underneath the participants’ lumbar regions, inferior to the occiput, and in the superior posterior aspect of the head. Velcro straps were fastened to the MRI table and used to secure the participant’s upper torso throughout the scan. Specifically, two straps were fastened bilaterally and stretched over the participant’s acromion process and sternum to the contralateral side of the abdomen, forming an X shape across the chest. Straps were also placed transversely over the sternum and over the anterior superior iliac spines. Our custom apparatus was also constructed with adjustable handlebars for participants to grip while in the MRI scanner. These handlebars were adjustable to be positioned for minimal elbow flexion. A Velcro head strap was fitted to the posterior aspect of the head coil and wrapped over the forehead to further limit head motion. A mirror was also positioned directly on top of the head coil to permit the participant full view of a projector screen for task-related instructions (Figure 1A).

The unilateral simulated landing task required the participants to flex their dominant (in this case all right) lower extremity to ~ 60-degree knee flexion along the track and then extending their lower extremity to ~ 0-degree knee flexion against resistance set at ~25% of body weight (0.25 × participant body mass = resistance of the band at full extension). The leg press apparatus slid superiorly or inferiorly to standardize the starting placement for all participants relative to individual anthropometrics. Pilot testing revealed that this resistance level was found to not be so high as to induce accessory motion artifact. The participant’s lower extremity movement resulted in the foot moving proximally along the track against the set resistance. The simulated landing device has two tracks, one for each leg, allowing independent unilateral movement. Following the 30s of rest with a blank screen in which the participant began fully extended, a visual countdown stimulus of “2”, “1” would appear on the screen followed by ‘move right’ for right leg or “move left” for left leg (all data reported

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herein are for the right dominate leg movement only) (Figure 1). Congruent with the onset of the ‘move right’ stimulus, a metronome (1.2 Hz) began which was audible to the participant through the headphones. The visual prompt of the countdown of “2” and “1” was designed to assure a smooth initiation and end of the move period in the fMRI paradigm. The participant was instructed to prepare to begin a slow and controlled movement upon viewing the ‘2’ stimulus and to start the motion in conjunction with the metronome starting when the move command was displayed. Near the end of the 30s move block, the participant would see “2”, “1”, indicating to prepare to stop moving followed by the stop command and participants would relax during the rest period (Figure 1). Akin to the move blocks, participants were instructed to slowly return to full extension when the ‘2’ stimulus appeared preceding the rest blocks to ensure a gradual, non-abrupt motion end to minimize head movement. To further minimize the potential for accessory head motion a complete familiarization session with examiner feedback on head motion was completed on a mock scanner prior to the actual MRI experiment. This familiarization session involved participants first watching a video of the task being completed, then completing the task in a mock scanner that simulated the same physical characteristics and noise of the actual MRI with the same auditory prompts and motor task. A researcher provided feedback during the familiarization session to minimize head motion and ensure task accuracy. All participants completed the same amount of familiarization (completed the entire movement paradigm once in the mock scanner) before actual scanning.

MRI data acquisition and analyses

All scans were performed on a 3T Philips Ingenia MRI scanner (Amsterdam, Netherlands) using a 32-channel head coil. An MPRAGE sequence was used to acquire high-resolution 3D T1-weighted images (sagittal): TR = 8.1 ms; TE = 3.7 ms; field of view = 256 × 256 mm; matrix = 256 × 256; in-plane resolution = 1×1 mm; slice thickness = 1 mm; number of slices = 180. The functional acquisition run consisted of four blocks of 30s cued contractions interleaved with five blocks of 30s rest periods (4:30 minute total scan time) which included 135 whole-brain gradient-echo echoplanar scans: TR = 2000 ms; TE = 35 ms; field of view = 240 × 240 mm; slice thickness = 5 mm; voxel size = 3.75mm × 3.75mm.

fMRI analyses were performed using the FSL software package (The Oxford Centre for Functional MRI of the Brain, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, United Kingdom[56] with standard processing. This included temporal high-pass filtering (90s), 4D mean intensity normalization, spatial smoothing at 6 mm FWHM, FILM prewhitening, slice timing correction, brain extraction and MCFLIRT motion correction and registration to participant anatomical and standard space via FNIRT.[30] First-level subject contrasts (knee movement – baseline [rest]) were completed with z threshold of 2.3 and $p < .05$ Gaussian random field cluster corrected.

Whole Brain Session Differences

To determine if our paradigm produced similar activation during both testing sessions, second-level between session contrasts (session 1 – session 2) were calculated with a z threshold of 3.5 and $p < .05$ Gaussian random field cluster corrected.[57,58] This higher-level session analysis was completed with FMRIB’s Local Analysis of Mixed Effects (FLAME)

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stage 1 and stage 259 using paired samples *t*-tests to contrast both sessions' whole brain activation (session one > session two & session two > session one).

Region of Interest Selection

In addition to examination of any differences in whole brain activity between the two sessions, a more in-depth analysis of key sensorimotor regions of interest (ROI) were also completed. ROIs were defined in a similar manner as previously described[60] and consisted of regions primarily involved in lower extremity motor control (right and left primary motor cortex, primary somatosensory cortex, pre-motor cortex, secondary somatosensory cortex, basal ganglia, and the cerebellum). The cerebellar ROI was created with the cerebellar atlas in MNI152 space after non-linear normalization and included all regions. The basal ganglia was created from the MNI structural atlas by combining the caudate and putamen. The Juelich Histological atlas was used to generate the other 8 cortical ROIs. The respective right and left primary motor cortex consisted of Brodmann area (BA) 4a (anterior) and BA 4p (posterior), primary somatosensory cortex consisted of BA1, 2, 3a and 3b, the secondary somatosensory cortex included BA OP (Operculum)1–4 in the parietal operculum and the pre-motor cortex entailed BA6. Second-level between session contrasts (session 1 – session 2) were calculated with a z threshold of 3.5 and $p < .05$ Gaussian random field cluster corrected as with the whole brain analysis, but masked for the 10 sensorimotor ROIs.[57,58] This higher-level session analysis was completed with FMRIB's Local Analysis of Mixed Effects (FLAME) stage 1 and stage 259 using paired samples *t*-tests to contrast both sessions' whole brain activation (session one > session two & session two > session one). A group by session average masked for the 10 sensorimotor ROIs was also completed to provide descriptive brain activity for the task.

Assessment of test-retest reliability

To estimate the reliability of brain activity within ROIs across sessions, we calculated the intraclass correlation (ICC) for the mean percent signal change and z-score for the anatomical ROI masked regions and computed a two-way mixed model ICC for absolute agreement. A paired samples t-test was also completed on each ROI's mean percent signal change and z-score in addition to the statistical parametric mapping described above to determine between session differences. ICC values were interpreted as excellent >0.75, good between 0.59 and 0.75, fair between 0.40 and 0.58, and poor if below 0.40.[61]

Results

All participants completed the leg press during sessions 1 and 2. The time between sessions ranged from 39 to 62 days with a mean of 49.69 (+/− 6.88) days equivalent to 7.10 (+/− 0.98) weeks. 5 of the 13 participants were excluded from the analysis for excessive mean head motion > 0.35 mm, while lower than the 0.5 mm previously reported,[26,60,62] was selected to ensure minimal influence of head motion on the brain activation profile (Table 1, head motion for all participants).

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Changes in Brain Activity between Sessions

At the whole-brain level there was no difference in the pair-wise statistical parametric mapping analysis between session 1 and session 2 nor were there differences when masked for the 10 sensorimotor ROIs. Regarding data extracted from each ROI, no differences in mean percent signal change were found for any ROI between session 1 and 2. Only the left cerebellum showed significantly decreased mean region z-score from session 1 to 2, with no other z-score differences.

Paradigm Brain Activation

Our leg press task was successful in inducing activation in all ten sensorimotor ROIs investigated including the cerebellum, basal ganglia, the right and left motor cortex, the pre-motor region, and the primary somatosensory and secondary somatosensory cortices (Figure 2, Table 2). Voxel total is the number of voxels in the anatomical region mask, active voxels are from the one sample t-test and represent the group-wise average number of voxels active during the task within the respective anatomical mask. The X, Y, Z location is for the group-wise peak voxel within the respective region.

Reliability of Brain Activity

The between-session ICCs for mean percent signal change in the ROI analysis were in the range between good to excellent (.621-.918) except for the left secondary somatosensory area which was poor (.165; Table 3). The ICC analyses for mean region z-score were all good to excellent (all > 0.697; Table 4).

Discussion

The purpose of this study was to present a novel method to assay brain activation during multi-joint lower extremity force production and attenuation while assessing the reliability of a loaded leg press across two-time points using fMRI. Our task was successful in inducing sensorimotor region activity to a similar degree as prior reports with lower extremity motor tasks.[60,62] The whole brain paired contrast revealed no differences in activation between sessions, and our ICCs indicated good to excellent reliability for the majority of investigated ROIs. Collectively, these results indicate our task is a reliable fMRI assay of neural function for lower extremity motor control.

Our reliability findings are in line with previous reports for similar motor paradigms of the lower extremity.[26,60] A previous isometric set-up achieved ICCs ranging from 0.29 to 0.74 for the contralateral sensorimotor cortex and 0.38 to 0.83 for the contralateral pre-motor cortex for low force knee extension contractions.[26] Our results were comparable with a 0.900 ICC for percent signal change in the contralateral motor and pre-motor cortices and 0.856 for motor cortex mean z-score and .867 for pre-motor region z-score. We attribute the improved ICC for our unilateral leg press to the participant familiarization session and differences in patient restraint and apparatus differences. Prior works using an isometric force generation task may have induced accessory head translation as the foot was fixed, but the force being generated may translate the body slightly, whereas in our task the foot moved on tracks and thus force production by the lower extremity musculature translated into hip

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and knee motion.[26] A comparable reliability study examining a stepping-like action machine found comparable ICCs with the present findings across the cerebellum, motor cortex, sensory cortex, and motor planning regions (0.70–0.85).[60] Our results differed regarding the secondary somatosensory region, specifically the left side for percent signal change having low reliability, whereas the previous investigation reported an ICC of .85 in the secondary somatosensory area between sessions.[60] One key difference is our paradigm was completed unilaterally compared to the bilateral active stepping motor paradigm engaging both legs reported by Jaeger et al.[24,60] The bilateral task may induce more reliable secondary sensory region activity bilaterally and facilitate a more uniform sensory experience between legs relative to the unilateral movement reported herein. Also, our participants completed task familiarization before each session, thus the overall novelty and attention during the actual scanning session may influence brain activity compared to prior studies that did not have familiarization sessions.[63]

Our results indicating high reliability for measuring neural activation for a loaded leg press have important implications for a variety of clinical populations. Leg press related exercises have been shown to improve healing after knee ligament injury and reconstruction surgery,[64] reduce pain and increase quadriceps strength in osteoarthritis,[65] and reduce pain in patellofemoral pain syndrome.[66] Thus, a reliable neuroimaging leg press paradigm could provide a neural assay to examine the neural mechanisms contributing to improved motor control or identify barriers in nonresponses for clinical populations with lower extremity musculoskeletal disorders. Further, such a paradigm can identify possible neural activity contributing to dysfunctional movement in those with injury.[67] As prior investigations have reported altered motor cortex excitability with transcranial magnetic stimulation and brain activation patterns for engaging the quadriceps muscle after knee joint injury,[68] this multi-joint leg press motion may provide further insights into the neuroplasticity for motor control related to joint injuries. Also, the good to high reliability provides a foundation for studying changes in neural function related to neuromuscular training and rehabilitation, providing neurophysiologic therapeutic targets in addition to the current standard of muscle or functional targets. For instance, decreased motor cortex activity during a loaded leg press exercise was correlated with improved landing mechanics measured during a virtual reality soccer task following real-time biofeedback training.[69] The reported changes in motor cortex activity can be safely attributed to the training, as opposed to limitations related to task reliability, especially as the contralateral motor cortex, in this case, had an excellent ICC of .9 for signal change and .86 for z-score between sessions.

While there were no condition differences in the group-wise statistical parametric mapping analysis, the left cerebellum approached significance for percent signal change and was significant for mean z-score in the ROI analysis. We attribute this difference to the nature of the cerebellar ROI analysis encompassing the entire left cerebellum and potentially being contralateral to the movement and thus not the primary cerebellar structure involved as the right cerebellum was less variable, having no pairwise difference. Prior work also found the cerebellum to be less consistent across sessions,[60] which found cerebellar activity to be the least reliable with ICCS ranging from 0.53–0.77, with our ICCs comparable or better despite the pair-wise difference. Thus, due to the varied structural and functional nature of the cerebellum, a sub-region may have higher reliability. To that end we ran a pairwise

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difference analysis between session 1 and session 2 on only the cerebellar regions found to be active during session 1 as opposed to the region as a whole and found no difference in z-score between sessions: session 1: 0.61 (.63); session 2: 0.55 (.41), $p = 0.70$. Therefore it is possible that the difference found above is due to including the entire left cerebellum, rather than more specific cerebellar ROIs.

The amount of head movement during the leg press task was measured to be 0.24 mm of absolute motion and 0.07 mm of relative motion, indicating that the majority of the brain stayed within the original voxel space throughout the task. In addition, 5 subjects (38%) had to be excluded from the study, which is lower than the 50% exclusion rate found when assessing the reliability of a fMRI passive stepping task.[60] This is likely due to the methods utilized to prevent head motion, including using physical restraints (e.g. straps), making the subject comfortable (e.g. lumbar support), and having familiarization sessions prior to the fMRI where the researcher strongly emphasized the importance of keeping the head stationary for the duration of the study in addition to task familiarization. Importantly, the amount of head motion elicited during our gross motor multi-joint movement is comparable to the amount of head motion observed during fine motor single joint movements in which physical restraints, physical comfort, and familiarization sessions are either not used, or less emphasized.

Beyond the novelty of the methods, a strength of this investigation was the repeated measurements being separated by a 7–8 week control period, providing implications for longer-term intervention measurement reliability. The ICCs evaluated in the proposed fMRI metrics were high and associated with consistent ROIs neural activity corresponding to this functional lower extremity movement. The stability of the measured sensorimotor outcomes over an extended period further enhances the clinical validity of the measurements beyond analytical validity commonly evaluated in reliability studies (e.g. within session or day to day reliability). Cumulatively the current data indicate that the proposed methods and metrics are viable outcomes to assess in longitudinal studies of injury risk and the potential effects of therapeutic interventions that aim to optimize movement efficiency and safety.

A limitation of this study was that the leg muscle activation and movement kinematics were not quantified simultaneously. While it would have been beneficial to correlate the brain activation pattern with muscle activation or temporal-spatial leg position, the task was auditory paced and set in tracks with blocks to ensure equivalent timing and range of motion across participants, thereby standardizing kinematic performance. However, these methods providing reliable assessment over time creates the opportunity to merge our MRI-safe leg press task with measurements of leg muscular activity and or a motion capture system.[70] A second limitation was that we completed this study utilizing a homogeneous population of female adolescent athletes, which limits our generalizability to other populations but does minimize confounding factors of gender and age. This decision to examine female adolescents specifically was done as knee joint injuries such as ACL rupture occur at a much greater rate in females[71–73] and is potentially due to unique neural activity related to knee motor control,[74] supporting the need to understand knee motor related neural activity in females. Nevertheless, testing the reproducibility of this task in other populations is warranted. It is also possible that task-related hand movements may have contributed to the

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reported neural activity, as participants were instructed to keep their hands on the handles for stability. Our ROI analysis did include the medial and lateral primary and secondary sensory and motor cortices, and as the ICCs were still high any participant-level variability in any task-related hand motion did not seem to impact the neural activity reliability. Despite these limitations, this study demonstrates the feasibility in measuring brain activation patterns during a loaded leg press exercise with mostly good to excellent reliability, indicating the utility of the task as a neuroimaging assay for lower extremity motor control. Future investigations should consider refinements to this paradigm with event-related designs and kinematic or kinetic recordings during scanning.

In conclusion, a loaded multi-joint unilateral leg press action that simulates the joint ranges of motion for squatting, stepping, stair climbing and landing from a jump is a reliable motor neuroimaging paradigm over a 7–8 week period.

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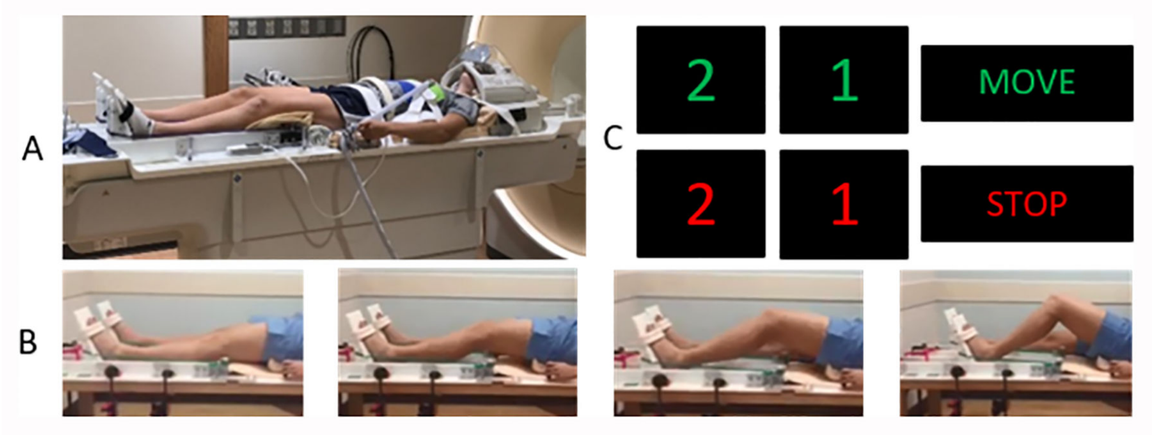

Figure 1.

A: Participant set-up in the MRI, with body straps to reduce accessory movement and demonstrating the leg press set-up. B: Participant completing the leg press motion. C: The visual prompts with a 2, 1 countdown to start moving and stop moving. The 2, 1 was provided to ensure participants were prepared to start moving and to stop.

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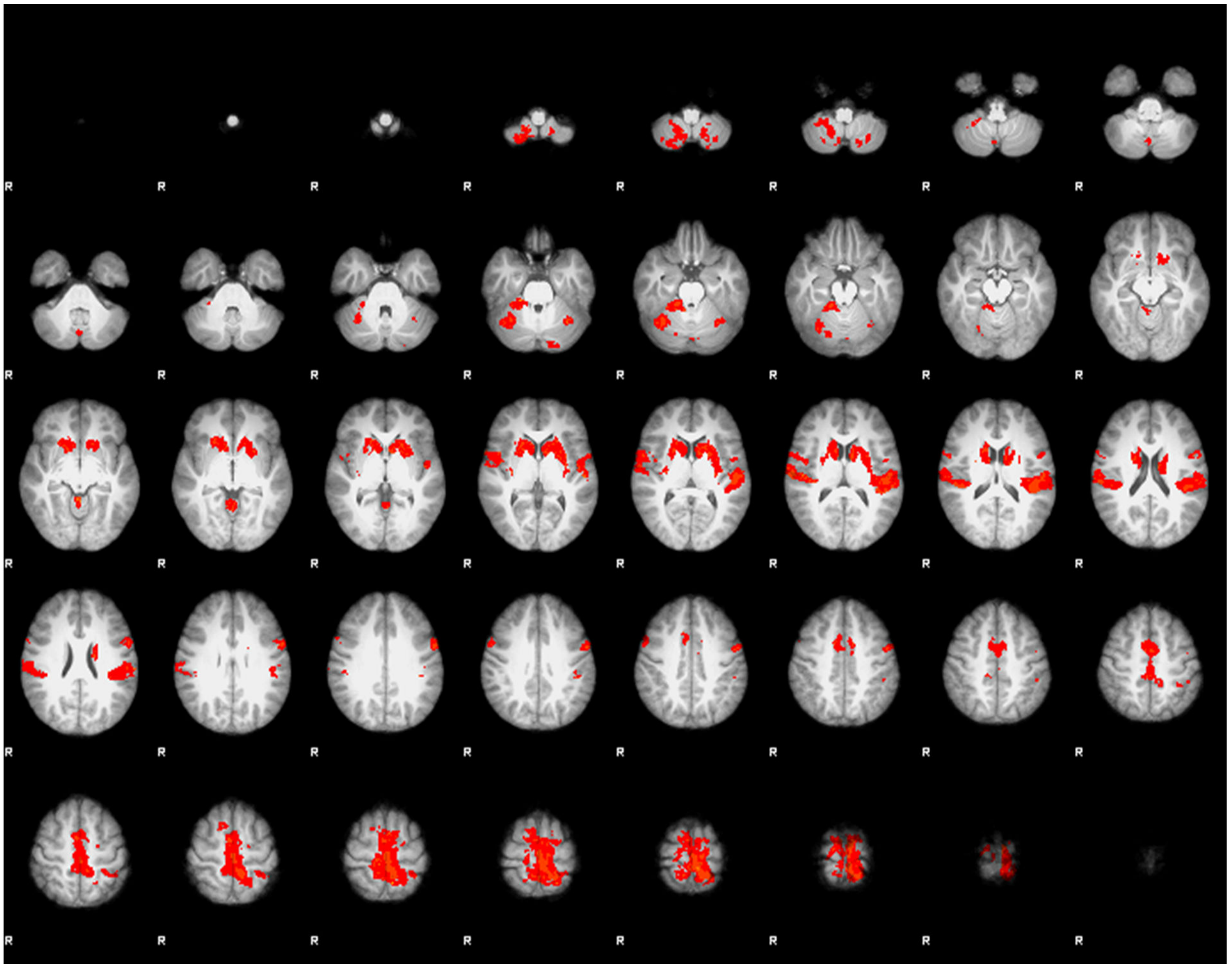

Figure 2.

Z-statistic activation map for the average combined session 1 and session 2 for the unilateral right leg press within the 10 a priori selected sensorimotor regions of interest. No differences in brain activity were found between session 1 and 2.

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Table 1.

Absolute and relative head motion for all participants.

Participant	Session 1 Absolute Head Motion (mm)	Session 1 Relative Head Motion (mm)	Session 2 Absolute Head Motion (mm)	Session 2 Relative Head Motion (mm)
Participant_01 *	0.6	0.1	0.26	0.06
Participant_02	0.24	0.06	0.22	0.05
Participant_03	0.14	0.04	0.21	0.05
Participant_04	0.22	0.09	0.26	0.09
Participant_05	0.21	0.07	0.21	0.06
Participant_06 *	0.46	0.09	0.16	0.05
Participant_07	0.29	0.08	0.28	0.06
Participant_08	0.28	0.09	0.25	0.1
Participant_09	0.24	0.09	0.22	0.06
Participant_10 *	0.8	0.15	0.4	0.11
Participant_11 *	0.39	0.08	0.27	0.07
Participant_12 *	0.52	0.12	0.24	0.07
Participant_13	0.31	0.11	0.23	0.08
Average ± Standard Deviation for entire group	0.34±0.19	0.09±0.03	0.25±0.06	0.07±0.02
Average ± Standard Deviation for those analyzed	0.24±0.05	0.08 ± 0.02	0.24±0.03	0.07±0.02

*dropped for excessive head motion beyond a priori established 0.35 mm

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Table 2.

Sensorimotor region activity metrics during the right leg press.

Region of interest	Voxels Total	Active Voxels	Mean % signal change (standard deviation)	Peak % Signal Change	Mean Z-score (standard deviation)	Peak Z-score	MNI Standard Space		
							X	Y	Z
Right Motor Cortex	5506	1030	0.25 (0.70)	3.65	0.61 (2.63)	6.06	2	−18	76
Left Motor Cortex	6297	2212	0.77 (1.31)	7.01	1.50 (2.75)	9.78	−6	−46	80
Right Pre−Motor Cortex	8732	1586	0.35 (0.70)	4.56	1.21 (2.36)	6.06	2	−8	74
Left Pre−Motor Cortex	8592	2420	0.74 (1.15)	8.65	1.96 (2.13)	9.78	−8	−12	80
Right Primary Somatosensory Cortex	6997	641	0.12 (0.53)	3.10	0.27(2.30)	6.05	8	−50	80
Left Primary Somatosensory Cortex	8103	1985	0.45 (0.98)	7.01	1.28 (2.55)	9.78	−6	−46	80
Right Secondary Somatosensory Cortex	3555	1276	0.54 (0.55)	2.98	2.26 (2.04)	7.42	62	8	2
Left Secondary Somatosensory Cortex	3661	1638	0.64 (0.59)	2.95	2.73 (1.92)	6.13	−66	−20	16
Right Cerebellum	10278	1540	0.52 (0.58)	4.34	1.67 (1.57)	7.75	32	−50	−58
Left Cerebellum	8790	415	0.29 (0.41)	2.85	0.99 (1.30)	6.81	−12	−60	−62
Right Basal Ganglia	2656	1147	0.37 (0.25)	1.44	2.88 (1.44)	5.92	12	22	−10
Left Basal Ganglia	2680	1485	0.44 (0.23)	1.50	3.26 (1.36)	5.80	−10	−4	16

Data presented below is the combined session group average as no differences were found between sessions.

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Table 3:

Intraclass Correlation Coefficient for % Signal Change between sessions for each sensorimotor region of interest

Region of Interest	Mean (standard deviation) Session 1	Mean (standard deviation) Session 2	p-value for difference	Intraclass Correlation Coefficient	Intraclass Correlation Coefficient p-value
Right Motor Cortex	0.25 (0.52)	0.23 (0.43)	.858	.834	.020
Left Motor Cortex	0.76 (0.48)	0.76 (0.41)	.989	.900	.005
Right Pre-Motor Cortex	0.41 (0.43)	0.43 (0.40)	.891	.811	.028
Left Pre-Motor Cortex	0.87 (0.56)	0.84 (0.36)	.820	.900	.005
Right Primary Somatosensory Cortex	0.18 (0.34)	0.09 (0.30)	.800	.879	.008
Left Primary Somatosensory Cortex	0.46 (0.36)	0.39 (0.30)	.412	.878	.007
Right Secondary Somatosensory Cortex	0.66 (0.31)	0.52 (0.18)	.156	.621	.088
Left Secondary Somatosensory Cortex	0.70 (0.34)	0.68 (0.17)	.896	.165	.419
Right Cerebellum	0.76 (0.57)	0.44 (0.50)	.114	0.772	.033
Left Cerebellum	0.81 (0.72)	0.32 (0.78)	.083	0.662	.052
Right Basal Ganglia	0.36 (0.30)	0.43 (0.22)	.167	.918	.001
Left Basal Ganglia	0.41 (0.39)	0.51 (0.24)	.315	.772	.033

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Table 4:

Intraclass Correlation Coefficient for Z-stat between sessions of each region of interest

Region of Interest	Mean (standard deviation) Session 1	Mean (standard deviation) Session 2	p-value for difference	Intraclass Correlation Coefficient	Intraclass Correlation Coefficient p-value
Right Motor Cortex	0.31 (0.80)	0.42 (1.01)	.676	.831	.020
Left Motor Cortex	1.25 (0.76)	1.47 (1.08)	.381	.856	.011
Right Pre-Motor Cortex	0.60 (0.79)	0.94 (0.95)	.239	.775	.029
Left Pre-Motor Cortex	1.34 (0.80)	1.70 (0.89)	.085	.867	.004
Right Primary Somatosensory Cortex	0.04 (0.60)	0.14 (0.77)	.590	.871	.009
Left Primary Somatosensory Cortex	0.82 (0.62)	0.94 (0.88)	.547	.883	.007
Right Secondary Somatosensory Cortex	1.35 (0.71)	1.15 (0.53)	.343	.776	.033
Left Secondary Somatosensory Cortex	1.46 (0.70)	1.70(0.69)	.302	.774	.032
Right Cerebellum	0.91 (0.78)	0.53 (0.60)	.138	.697	.049
Left Cerebellum	0.81 (0.93)	0.33 (0.76)	.016	.864	.001
Right Basal Ganglia	0.94 (0.70)	1.02 (0.57)	.619	.870	.010
Left Basal Ganglia	1.00 (0.79)	1.27 (0.66)	.203	.810	.017