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Focus of Attention Impacts Brain Activity and Connectivity early after Anterior Cruciate Ligament Reconstruction

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Context: Individuals who undergo anterior cruciate ligament (ACL) reconstruction (ACLR) have altered sensorimotor brain activity that can persist for years. Directing an individual's focus of attention (FoA) using instructional cues during rehabilitation and motor control training can impact movement performance but the direct effects on sensorimotor brain activity and network level relationships in an ACLR population are less understood. This can have important implications for understanding the neural underpinnings of automatic control processes for direct application to motor learning.

Objective: Determine differences in brain activity and patterns of activity when ACLR knee movement is cued using an internal FoA (iFoA) compared to an external FoA (eFoA).

Design: Cross-sectional study.

Setting: Research laboratory.

Patients or Other Participants: We recruited 12 participants (7 females, 6.9 ± 1.0 weeks post-ACLR) after primary, unilateral, ACLR. Participants performed repeated isometric quadriceps contractions under iFoA and eFoA conditions during functional magnetic resonance imaging scans.

Main Outcome Measures: Brain activity (blood oxygen level dependent response) from anatomic regions of interest were extracted from move-rest contrasts in each FoA condition and paired t-tests determined differences in activity across conditions. Intra and inter-network connectivity analyses were performed using MELODIC ICA. Dual regression and fsl *randomise were used* to determine differences in network connectivity between iFoA and eFoA conditions.

Results: The eFoA condition elicited greater activity in precuneus compared to the iFoA condition. Default Mode Network (DMN) demonstrated greater intra-network connectivity in the eFoA condition compared to iFoA in precuneus and lateral occipital cortex.

Conclusion: Increased precuneus activity may be a favorable adaptation for motor performance and greater within DMN connectivity could indicate more optimal network organization to improve motor efficiency and support automation. This suggests that automatic control processes may be facilitated neurologically by eFoA, reducing the attentional demand to perform basic knee movement after ACLR.

Key Words: ACLR, Brain Activity, fMRI, Sensorimotor, Motor Control

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Key Points

- Performing quadriceps isometric contractions with an external focus of attention increases brain activity in precuneus, a brain region important for sensorimotor adaptation after ACLR
- External focus of attention promotes a more automatic control of movement when compared to an internal focus of attention
- External focus of attention may help to improve motor learning efficiency after ACLR

Individuals who undergo anterior cruciate ligament (ACL) reconstruction (ACLR) have altered sensorimotor brain activity that persists for years after medical clearance for full return to activity.[1] Brain activity changes, identified using functional magnetic resonance imaging (fMRI), occur within regions traditionally associated with sensorimotor function, such as primary motor cortex (M1) and somatosensory cortex (S1).[1] Regions not typically associated with sensorimotor function, such as lingual gyrus, also differ after ACLR compared to controls during a knee motor control task.[1] Another non-traditional region with involvement in post-ACLR sensorimotor function is precuneus. Activity in precuneus during knee motor control is associated with sport-relevant performance indicators[2,3] years after ACLR. Brain activity during rehabilitation has been less studied, but preliminary work identified widespread frontal cortex changes in response to a non-ACLR limb intervention from two to ten weeks post-operatively.[4] Our prior work investigated individuals seven weeks after ACLR and found reduced activity in M1, S1, supplementary motor area (SMA) and precuneus during knee motor control compared to control individuals.[5] The collective findings from our prior work and others suggest motor control associated brain activity changes after ACLR occur within traditional and non-traditional sensorimotor regions.

Early-stage rehabilitation targets fundamental goals related to range of motion, pain, muscle activation, and swelling reduction.[6] Rehabilitation transitions to strength and motor pattern retraining between six and eight weeks post-operatively.[6] This is an important rehabilitation window when individuals are actively engaged in motor learning to build the foundational movement patterns needed for strength training and future sport-related movements. Integrating motor learning principles into rehabilitation promotes better motor pattern retention and movement efficiency.[7] Effective motor learning propagates faster advancement through motor learning stages, allowing rehabilitation providers to layer advanced challenges, such as dual task, or to address other movement pattern deficiencies. Focus of Attention (FoA) is a motor learning concept which brings a specific task component to conscious awareness[8] and assessing how brain activity is impacted by an individual's FoA during motor control can provide insight on the neurologic processes affected by this concept of motor learning.

An internal FoA (iFoA) occurs when instructional cues emphasize particular body movements or limb segments.[8] An external FoA (eFoA) occurs when attention is directed to the action's outcome or impact on the environment.[8] Instructing a motor task using eFoA improves motor performance, skill retention, biomechanics, movement accuracy, consistency, and efficiency when compared to an iFoA.[8] The constrained-action hypothesis suggests an iFoA disrupts automatic control processes, the natural regulation of an individual's movement when conscious awareness of the movement is reduced.[9] An eFoA reduces conscious awareness, facilitating automatic control processes and promoting natural self-organization of the motor system.[9] Rehabilitation after ACLR often hyperfocuses on the individual's knee, bringing it to conscious awareness, and potentially interfering with automatic control processes. When assessed in a healthy population, eFoA elicits greater activity in the ventral stream, responsible in part for visual identification, while iFoA increases activity in M1 and other regions associated with motor planning and feedback.[10] This suggests iFoA and eFoA cues could be applied in a targeted fashion to address specific neurologic mechanisms in healthy adults, but whether FoA manipulation targets similar mechanisms after ACLR is unknown. Therefore, identifying whether iFoA and eFoA create similar neurologic responses in individuals after ACLR can aide in the selection of cueing strategies to selectively impact brain activity during rehabilitation.

Facilitating automatic control processes is thought to reduce cognitive interference or the neural resources required to perform a motor task,[9] promoting neurologic efficiency of movement.[4,10] Movement performed with greater neurologic efficiency may impact brain activity magnitude or how brain networks interact with one another. Sensorimotor network may respond differently to FoA conditions given an eFoA benefits many aspects of motor performance[8] and brain activity during motor control is different after ACLR compared to controls.[1] FoA may also impact movement awareness which can be assessed by default mode network (DMN). DMN is comprised of regions throughout the brain which are active while an individual is awake and alert but not attending to any specific stimuli.[11] DMN activity reduces when a person is engaged in a goal-directed task, and further deactivates with increasing task complexity and difficulty.[12] Healthy college students demonstrate greater DMN connectivity during a force control task when cued using an eFoA condition compared to iFoA condition, and connectivity was associated with better task accuracy,[13] suggesting greater DMN connectivity has motor performance benefits. Evaluating DMN and sensorimotor network connectivity will deepen understanding of how cognitive FoA impacts relevant brain network relationships during sensorimotor control after ACLR.

The purpose of our study was to identify differences in brain activity (measured by the blood oxygen level dependent (BOLD) response) and patterns of activity during ACLR limb isometric quadriceps contractions when cued using an iFoA compared to an eFoA. Our primary hypothesis was that the eFoA condition would elicit different magnitudes of brain activity in

M1, S1, SMA, precuneus and lingual gyrus compared to the iFoA condition. Our secondary hypothesis was the eFoA condition would induce greater intra- and inter-network functional connectivity of sensorimotor network and DMN.

METHODS

Participants

We recruited twelve individuals (7 females, 5 males) after primary, unilateral, ACLR for participation and individuals provided written informed assent and parental permission for minors, or informed written consent prior to study participation XXX. We recruited potential participants via electronic medical record review and word of mouth at XXX between May 5, 2021 and December 28, 2023. Enrolled participants had a mean age of 22.3 ± 3.9 years old and were 6.9 ± 1.0 weeks post-ACLR (graft types: 8 patellar tendon autografts, 4 hamstring autografts; self-reported limb dominance: 11 right, 1 left; laterality of injury: 3 right, 9 left) at the time of participation. We screened participants with the following criteria;

Inclusion Criteria:

1. Primary, unilateral ACLR
2. Actively engaged in rehabilitation and progressing without major knee motion deficits per the clinical practice guidelines outlined by XXX
3. Tegner Level of Activity ≥ 6 prior to injury.
4. Age 15-30 years

Exclusion Criteria:

1. Concomitant surgical procedure aside from debridement, meniscal repair, or meniscectomy

2. Prior spine or lower extremity surgery (including ACL graft revision or contralateral ACLR)
3. Surgery or rehabilitation performed outside of XXX network of providers
4. Current or prior medical treatment for neurologic disorders
5. Embedded ferrous material (MRI compliance criteria)
6. Pregnancy (MRI compliance criteria)

Task and Procedure

Participants performed two, 4-minute runs of repetitive isometric quadriceps femoris muscle contractions in anatomic position with standard padding to improve comfort and assist in reducing head motion. Prior to functional scanning, we placed a sticker on the popliteal fossa of the participant's ACLR knee to be used during the eFoA condition to prevent differences in tactile stimuli contributing to activity differences during the task. Run 1 consisted of the iFoA condition and run 2 the eFoA condition, order of performance was not randomized as this was a proof-of-concept design. Participants were familiarized with the instructions prior to each run and were asked if they needed clarification on instructions, no other rest was provided. For the iFoA condition, we cued participants prior to scanning to "flex your quad(riceps muscle)" and for the eFoA condition, we cued participants to "press the sticker into the table". During scanning, the words "flex" or "press" appeared on a screen viewed by the participant through a mirror to signify the start time, and "2, 1, STOP" was presented in red to end each block for both conditions. Participants performed 20 seconds(s) of movement alternating with 20s of rest in a blocked design, each run consisted of 12 total blocks, 6 blocks of movement and 6 blocks of rest. During the movement block, pace of movement was cued by an auditory metronome at

1.2Hz. We asked participants if they experienced pain during task performance after each condition, no participants reported pain.

fMRI Data Acquisition and Analysis

We collected data using a 3T Siemens MAGNETOM Prisma Scanner (Siemens AG, Munich, Germany) with a 32-channel head coil. We collected a T1-weighted MPRAGE sequence (voxel resolution of $0.8mm^3$) for registration of functional images to Montreal Neurological Institute (MNI) 152 standard template. Our functional scanning parameters were: repetition time (TR) = 1000ms, echo time (TE) = 28ms, volumes = 270, multi-band factor = 3, field of view (FoV) = 210mm, slice thickness = 3.0mm, voxel resolution = $3.0mm^3$. We processed and analyzed the data using FSL 6.1 (FMRIB, Oxford, UK). Preprocessing steps included brain extraction, motion correction, slice timing correction, spatial smoothing (5mm FWHM Gaussian kernel), intensity normalization, linear registration to the T1 anatomic image using full search and 6 degrees of freedom (DoF), and non-linear registration to MNI 152 standard template using a 10mm warp. We completed denoising and signal variation reduction using independent component analysis for automatic removal of motion artifact (ICA-AROMA)[14] with non-aggressive denoising, followed by high pass temporal filtering at 100Hz. FSL's FMRIB's Automated Segmentation Tool (FAST)[15] performed individual anatomic brain tissue segmentation to create cerebrospinal fluid masks which we included as nuisance regressors in subsequent analysis. Move minus (-) rest contrasts were performed by modeling the BOLD response (brain activity) during movement and rest blocks, then subtracting out rest activity from movement activity at the subject level, for each FoA condition separately**.** Subject level data were multiple comparisons corrected using cluster-based thresholding set at z = 3.1, and alpha level set *a priori* at $\alpha = 0.05$.

Region of Interest (ROI) Creation

Following methods used in our prior work,[5] anatomic masks were generated for right and left M1, right and left S1, and SMA using the Juelich Histologic Atlas.[16] Creating masks in this manner allows us to assign these regions as contralateral and ipsilateral, relative to the individual's laterality of ACLR. Masks for precuneus and lingual gyrus were created using the Harvard-Oxford Cortical Atlas,[17] and were created bilaterally as it's unclear whether these regions demonstrate the same hemispheric specificity as M1 and S1. Probability thresholds were set at 50% to define all anatomic regions.[18] **Fig. 1** depicts the regions of interests on an MNI152 standard brain template.

Place Fig. 1

Mean percent signal change data were extracted from all ROIs using FSL's Featquery function from the move-rest contrast of parameter estimates. Extracted activity data were thresholded to include only voxels which increased in activity during the move-rest contrast. This step was performed to ensure only task active voxels were analyzed to further restrict anatomic ROI sizes and capture only data relevant to motor control. Data were averaged at the group level and paired samples t-tests were used to determine differences in brain activity between the eFoA and iFoA conditions. Data are presented in the results using an uncorrected alpha level for significance testing, $\alpha = 0.05$ and also with Bonferroni adjusted contrasts for multiple comparisons correction. We used Cohen's d to calculate effect sizes and they were interpreted as small, medium or large at $d = 0.20$, 0.50, and 0.80, respectively.[19]

Network Connectivity Analysis

Group-level Multivariate Exploratory Linear Optimized Decomposition into Independent Components (MELODIC) independent component analysis (ICA) was performed restricted to 5 to 12 dimensions to evaluate network components. Components were correlated to pre-established network templates[20] to determine appropriate dimensionality. These pre-established brain network templates were derived from the BrainMap database containing data from >1600 published articles using task-based analyses, representing 19% of all published fMRI data at the time of map creation.[20] The highest correlation between the template and MELODIC identified sensorimotor network (r=0.45) and template and MELODIC identified DMN (r=0.50) occurred at 10 dimensions. This approach was chosen over seed-based connectivity analyses, such as psychological-physiological interaction, allowing a data-driven approach for sensorimotor network and DMN definition, and to assess networks independently from one another.

Stage 1 and 2 dual regression was performed using the fsl command *dual_regression*. Briefly, stage 1 uses group-average spatial maps as regressors to generate each subject's data timeseries and stage 2 uses the subject specific time-series data as a temporal regressor to generate a subject-specific spatial map.[21] Inter- and intra-network functional connectivity was evaluated by non-parametric permutation testing with 5000 permutations per analysis with the fsl command *randomise.* Four separate analyses (two inter- and two intra-network) were performed on the sensorimotor network and DMN components from the group-level MELODIC ICA. For inter-network connectivity, a whole brain MNI 152 template mask was used in the *randomise* command with the respective network (Sensorimotor or DMN) to determine how the entire brain's network connectivity differs between conditions. For intra-network connectivity of each network, a z-threshold (z = 3.1) and binarized network mask was used to constrain the analysis to areas within the network only. Statistical thresholding was multiple comparisons corrected using cluster-based thresholding set at z = 3.1, and alpha level set *a priori* at $\alpha = 0.05$.

RESULTS

ROI Analysis

The eFoA condition elicited greater activity in precuneus compared to the iFoA condition (0.32 ± 0.10% vs. 0.23 ± 0.11%, $t(11) = 3.24$, $p = 0.008$, $d = 0.88$). However, this result did not survive multiple comparisons correction using Bonferroni adjusted contrasts, p = 0.056. There were no statistically significant differences between conditions for right or left M1, right or left S1, SMA or lingual gyrus. Individual data points can be visualized in **Fig. 2** and statistics can be found in **Table 1**

Place Fig. 2

Place Table 1

Network Connectivity Analysis

There were no differences in sensorimotor intra-network connectivity (eFoA>iFoA, p = 0.35, eFoA<iFoA, p = 0.17) or inter-network connectivity (eFoA>iFoA, $p = 0.34$, eFoA<iFoA, $p = 0.20$) between FoA conditions. The intra-network connectivity analysis for the DMN revealed greater connectivity in the eFoA condition compared to iFoA in precuneus (size = 186 voxels, peak significance voxel = 0.03, peak significance voxel location: X = 44, Y = 31, Z = 40) and lateral occipital cortex (size = 177 voxels, peak significance voxel = 0.03, peak significance voxel location: X = 67, Y = 23, Z = 43), see **Fig. 3** for clusters and the MELODIC identified DMN.

Place Fig. 3

There were no differences for DMN intra-network connectivity for the eFoA<iFoA contrast (p = 0.23) or inter-network connectivity for DMN (eFoA>iFoA, p = 0.15, eFoA<iFoA, p = 0.30).

DISCUSSION

The purpose of this study was to quantify brain activity and network connectivity changes during quadriceps muscle contractions cued with an iFoA compared to eFoA. The ROI analysis revealed greater activity in precuneus during the eFoA condition compared to iFoA condition. This result did not survive multiple comparisons correction but the difference in percent signal change between conditions does represent a large effect size, therefore this may be a meaningful difference. There were no differences in right or left M1, right or left S1, SMA, or lingual gyrus activity across conditions. These results did not support our hypothesis that an eFoA would elicit greater widespread activity in our sensorimotor ROIs. The network level analyses identified no changes to intra or inter-network connectivity for sensorimotor network across our FoA conditions, contrary to our secondary hypothesis. Greater intra-network connectivity was identified within DMN; precuneus and lateral occipital cortex (regions within DMN) had greater connectivity to the rest of DMN during the eFoA condition compared to the iFoA condition which was in support of our secondary hypothesis.

A large effect size in precuneus for the eFoA > iFoA contrast indicates manipulating FoA could be a meaningful strategy for impacting real-time brain activity in this region after ACLR. Precuneus plays a role in motor imagery and in spatially oriented movements, [22] and prior work identified decreased activity in precuneus early after ACLR compared to a control group,[5] but there is limited additional evidence to contextualize our precuneus activity early after ACLR.

Individuals who were years removed from their ACLR demonstrate greater precuneus activity during motor control, which was associated with better visual motor performance[2] and better knee-related biomechanics during a change of direction task.[3] Therefore a long-term neuroplastic change upregulating precuneus activity may be favorable, but additional work is needed to confirm this relationship. It is important to note that our effect could be driven by task order, as the iFoA run was performed prior to the eFoA run for all participants, and brain activity is impacted by repetition. However, there was no consistent directionality in our results (e.g. eFoA > iFoA in all ROIs), SMA had higher, non-significant, activity in the iFoA condition. Since SMA had higher mean activity in the iFoA condition, there does not appear to be a systemic demonstration of task order in our results, lessening these concerns.

No differences in M1, S1 or lingual gyrus activity across FoA conditions suggests these regions respond selectively to an isolated knee motor control task and are not sensitive to FoA manipulation in our cohort. This result is consistent with the known primary functions of M1 to execute movement and dictate muscle force generation.[23] Similarly, S1 responds to movement with a proportional activity response to the magnitude of sensory information it receives[24] which it directly communicates to M1. Therefore, no differences in M1 and S1 activation in response to our FoA paradigm corroborates these known functions as muscular force and tactile stimuli were not manipulated in our design. Lingual gyrus's role in motor control is less clear but it's believed to be involved in motor imagery,[25] cross-modal information processing[26] and has demonstrated increased activity during motor control after ACLR compared to healthy controls.[1] Our results again identified a lack of response in lingual gyrus and could suggest neither cross-modal processing nor motor imagery are impacted by our method of motor control FoA manipulation early after ACLR. However, this was not directly assessed and should be evaluated by a specific motor imagery paradigm in the future.

Prior work evaluating FoA's impact on motor control brain activity in uninjured active individuals identified greater activity in M1 and S1 in the iFoA condition and greater lingual gyrus activity in the eFoA condition,[10] contrasting our results. These differences may be attributed to methodological differences in our analysis technique and motor task. Our ROI analysis evaluates mean activity within a constrained anatomic region, whole-brain analysis allows for unique unrestricted activity configurations. Our paradigm included only different instructional cues creating an iFoA or eFoA, with no changes in visual or somatosensory stimuli across conditions. These methodological differences may account for our discrepant results, or may represent a difference between populations prompting future investigations to include both a control and ACLR population.

Network Connectivity

The lack of significant results for our sensorimotor intra- and inter- network connectivity analyses indicates manipulating FoA during quad sets does not impact correlations within network or correlations to other networks. This is a surprising result given other work has identified differences in electromyography quadriceps activity,[27] intracortical inhibition of M1[28] and widespread differences in motor, somatosensory, and parietal region activity across FoA conditions after ACLR.[29] Our results indicate that sensorimotor network connectivity relationships are unchanged across FoA conditions, despite prior evidence to suggest activity within sensorimotor network is impacted. This may indicate our FoA paradigm does not impact the synchronous relationship of sensorimotor brain activity, or our tasks were not robust enough to elicit a response. Our participants completed a highly familiar and simple task which may explain the lack of sensorimotor network differences across conditions.

Lateral occipital cortex and precuneus, regions within DMN, demonstrated greater connectivity to DMN in the eFoA condition compared to iFoA. Greater within DMN connectivity may indicate reduced cognitive attentional resources are required during eFoA which could benefit motor performance based on prior work.[13] This result suggests that automatic control processes are facilitated neurologically by eFoA, as proposed in the constrained action hypothesis,[9] since prior work indicates greater within DMN connectivity supports 'autopilot' behavior.[30] Functional connectivity between DMN and sensorimotor network is thought to be unaffected by the immediate external environment due to their anatomically distant locations from one another, providing some basis for a lack of result between sensorimotor network and DMN.[31] DMN's role is typically more prevalent when decisions are made from prior experience as opposed to real-time sensory information,[31] suggesting our eFoA condition may evoke some amount of motor memory recall or help encode motor memories as DMN assists with memory consolidation during sensorimotor adaptation.[32]

Implications for Motor Learning

Motor learning is understood in three stages. A new learner begins in the cognitive stage when more conscious thought and feedback is needed for skill improvement.[33] A learner moves to the associative stage where learning becomes less reliant on conscious thought, and errors are made and corrected with less frequent feedback.[33] Lastly, a learner enters the autonomous stage where motor performance becomes more automatic.[33] Due to the decreased cognitive effort the skill requires, learners are able to process secondary information and participate in more dual task activities.[34] The autonomous learning stage is particularly crucial for individuals after ACLR given the increased dual-task cost for balance, gait, cognitive performance,[35] and coordination[36] compared to controls. Individuals after ACLR re-learn how to perform muscle contractions, activities of daily living, functional movement patterns, weightlifting techniques and sport specific movements, all in the span of nine to twelve months.[37] Accelerating motor learning can facilitate performance improvements on specific motor tasks, allowing rehabilitation providers to layer on increased task complexity. This is especially relevant to our cohort who are on average 7 weeks post-ACLR and are being frequently exposed to movements in rehabilitation they have not performed since surgery. We hypothesize that using an eFoA for more basic tasks, i.e. quadriceps contractions as evaluated in this study, could help facilitate better performance of these tasks and potentially allow for a quicker progression to functional movements. Using the same eFoA strategy to then facilitate functional movements may optimize motor learning and should be evaluated for its effect on movement performance throughout rehabilitation as task complexity increases. These implications for motor learning may not be specific to individuals after ACLR, brain activity and activity patterns may be impacted similarly in other populations or in healthy individuals and our findings and hypothesis should be replicated in other populations.

Limitations

Limitations to the current study include the small sample size (n = 12) which provides limited power to our results. We recommend others to corroborate these results with larger samples. The order of FoA cue was not randomized as all participants performed the iFoA condition first. This may have unknown effects on the outcome, however, since only one ROI differed in activity across groups, this effect may be negligible. Our specific FoA verbal and visual cues were selected to mimic common language and techniques used by rehabilitation specialists and different instructional language may result in different brain activation patterns than we observed. We did not control for swelling or arthrogenic muscle inhibition which may also influence brain activation and activity patterns. Due to our lack of a control group, we are unable to conclude our results are unique to an ACLR population and therefore this may be an expected effect of FoA manipulation during a motor task in all individuals.

Finally, our ROI analysis accounted for laterality of injury, but our network level analyses did not. This is an important distinction from our ROI approach as percent signal change determines the magnitude of activity, compared to a network connectivity analysis which evaluates the correlation of activity change, not magnitude. This may have impacted our null results for sensorimotor network, although no prior work has evaluated this scenario. Regarding DMN, there is no direct theoretical basis to suggest differences in DMN connectivity during a motor task would be impacted by the laterality of limb movement. The DMN is a task negative network, increasing confidence that our results for the DMN intra-network analysis is an actual effect.

CONCLUSION

Our study identified that an eFoA cue elicits greater brain activity within precuneus compared to an iFoA cue during a lower extremity motor control task. These results add to a growing body of evidence supporting brain activity changes within precuneus after ACLR, related to adaptations in sensorimotor function. No differences in activity for bilateral M1, bilateral S1, SMA or lingual gyrus indicates these regions are not sensitive to cognitive FoA manipulation in our ACLR cohort which differs from prior work evaluating healthy active individuals.[10]

There were no differences for within sensorimotor network connectivity or for connectivity among sensorimotor and other brain networks when contrasting our FoA conditions. This indicates network level relationships in how the brain activates synchronously or asynchronously with sensorimotor network are unchanged by cognitive FoA manipulation. The intra-network connectivity analysis within DMN identified greater precuneus and lateral occipital cortex (regions within DMN) connectivity to the rest of DMN during the eFoA condition, suggesting that attentional demands during motor control are reduced by an eFoA. This study evaluated the effects of cognitive FoA manipulation in an ACLR population and provides novel insight on potential strategies to influence precuneus activity and DMN network connectivity which may have implications for motor learning during rehabilitation.

REFERENCES

1. Grooms DR, Page SJ, Nichols-Larsen DS, Chaudhari AMW, White SE, Onate JA. Neuroplasticity associated with anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther*. 2017;47(3):180-189. doi:10.2519/jospt.2017.7003

2. Chaput M, Onate JA, Simon JE, et al. Visual cognition associated with knee proprioception, time to stability, and sensory integration neural activity after ACL reconstruction. *J Orthop Res*. 2022;40(1):95-104. doi:10.1002/jor.25014

3. Culiver A, Grooms D, Edwards N, Schmitt L, Oñate J. A Preliminary Investigation into the Neural Correlates of Knee Loading during a Change of Direction Task in Individuals after Anterior Cruciate Ligament Reconstruction. *Int J Sports Phys Ther*. 2023;18(1):70-80. doi:10.26603/001c.57782

4. Lepley LK, Grooms DR, Burland JP, et al. Eccentric cross-exercise after anterior cruciate ligament reconstruction: Novel case series to enhance neuroplasticity. *Phys Ther Sport*. 2018;34:55-65. doi:10.1016/j.ptsp.2018.08.010

5. Culiver AM, Grooms DR, Caccese JB, Hayes SM, Schmitt LC, Oñate JA. fMRI Activation in Sensorimotor Regions at 6 Weeks After Anterior Cruciate Ligament Reconstruction. *Am J Sports Med*. Published online February 4, 2025:03635465251313808. doi:10.1177/03635465251313808

6. Buckthorpe M, Gokeler A, Herrington L, et al. Optimising the Early-Stage Rehabilitation Process Post-ACL Reconstruction. *Sports Med*. Published online October 3, 2023. doi:10.1007/s40279-023-01934-w

7. Gokeler A, Neuhaus D, Benjaminse A, Grooms DR, Baumeister J. Principles of Motor Learning to Support Neuroplasticity After ACL Injury: Implications for Optimizing Performance and Reducing Risk of Second ACL Injury. *Sports Med*. 2019;49(6):853-865. doi:10.1007/s40279-019-01058-0

8. Wulf G. Attentional focus and motor learning: a review of 15 years. *Int Rev Sport Exerc Psychol*. 2013;6(1):77-104. doi:10.1080/1750984X.2012.723728

9. Wulf G, McNevin N, Shea CH. The automaticity of complex motor skill learning as a function of attentional focus. *Q J Exp Psychol Sect A*. 2001;54(4):1143-1154. doi:10.1080/713756012

10. Raisbeck LD, Diekfuss JA, Grooms DR, Schmitz R. The Effects of Attentional Focus on Brain Function During a Gross Motor Task. *J Sport Rehabil*. 2019;29(4):441-447. doi:10.1123/jsr.2018-0026

11. Broyd SJ, Demanuele C, Debener S, Helps SK, James CJ, Sonuga-Barke EJS. Default-mode brain dysfunction in mental disorders: A systematic review. *Neurosci Biobehav Rev*. 2009;33(3):279-296. doi:10.1016/j.neubiorev.2008.09.002

12. Fransson P. How default is the default mode of brain function?: Further evidence from intrinsic BOLD signal fluctuations. *Neuropsychologia*. 2006;44(14):2836-2845. doi:10.1016/j.neuropsychologia.2006.06.017

13. Zhou ZW, Lan XQ, Fang YT, et al. The Inter-Regional Connectivity Within the Default Mode Network During the Attentional Processes of Internal Focus and External Focus: An fMRI Study of Continuous Finger Force Feedback. *Front Psychol*. 2019;10:2198. doi:10.3389/fpsyg.2019.02198

14. Pruim RHR, Mennes M, van Rooij D, Llera A, Buitelaar JK, Beckmann CF. ICA-AROMA: A robust ICA-based strategy for removing motion artifacts from fMRI data. *NeuroImage*. 2015;112:267-277. doi:10.1016/j.neuroimage.2015.02.064

15. Zhang Y, Brady M, Smith S. Segmentation of brain MR images through a hidden Markov random field model and the expectation-maximization algorithm. *IEEE Trans Med Imaging*. 2001;20(1):45-57. doi:10.1109/42.906424

16. Geyer S, Schormann T, Mohlberg H, Zilles K. Areas 3a, 3b, and 1 of Human Primary Somatosensory Cortex: 2. Spatial Normalization to Standard Anatomical Space. *NeuroImage*. 2000;11(6):684-696. doi:10.1006/nimg.2000.0548

17. Desikan RS, Ségonne F, Fischl B, et al. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *NeuroImage*. 2006;31(3):968-980. doi:10.1016/j.neuroimage.2006.01.021

18. Wang Y, Zhan M, Roebroeck A, De Weerd P, Kashyap S, Roberts MJ. Inconsistencies in atlas-based volumetric measures of the human nucleus basalis of Meynert: A need for high-resolution alternatives. *NeuroImage*. 2022;259:119421. doi:10.1016/j.neuroimage.2022.119421

19. Cohen J. *Statistical Power Analysis for the Behavioral Sciences*. 2nd ed. Routledge; 1988. doi:10.4324/9780203771587

20. Smith SM, Fox PT, Miller KL, et al. Correspondence of the brain's functional architecture during activation and rest. *Proc Natl Acad Sci U S A*. 2009;106(31):13040-13045. doi:10.1073/pnas.0905267106

21. Nickerson LD, Smith SM, Öngür D, Beckmann CF. Using Dual Regression to Investigate Network Shape and Amplitude in Functional Connectivity Analyses. *Front Neurosci*. 2017;11:115. doi:10.3389/fnins.2017.00115

22. Cavanna AE, Trimble MR. The precuneus: a review of its functional anatomy and behavioural correlates. *Brain*. 2006;129(3):564-583. doi:10.1093/brain/awl004

23. Omrani M, Kaufman MT, Hatsopoulos NG, Cheney PD. Perspectives on classical controversies about the motor cortex. *J Neurophysiol*. 2017;118(3):1828-1848. doi:10.1152/jn.00795.2016

24. Fortier-Poisson P, Langlais JS, Smith AM. Correlation of fingertip shear force direction with somatosensory cortical activity in monkey. *J Neurophysiol*. 2016;115(1):100-111. doi:10.1152/jn.00749.2014

25. Zhang H, Liu J, Zhang Q. Neural representations for the generation of inventive conceptions inspired by adaptive feature optimization of biological species. *Cortex*. 2014;50:162-173. doi:10.1016/j.cortex.2013.01.015

26. Macaluso E, Driver J. Spatial attention and crossmodal interactions between vision and touch. *Neuropsychologia*. 2001;39(12):1304-1316. doi:10.1016/S0028-3932(01)00119-1

27. Zachry T, Wulf G, Mercer J, Bezodis N. Increased movement accuracy and reduced EMG activity as the result of adopting an external focus of attention. *Brain Res Bull*. 2005;67(4):304-309. doi:10.1016/j.brainresbull.2005.06.035

28. Kuhn Y -A., Keller M, Ruffieux J, Taube W. Adopting an external focus of attention alters intracortical inhibition within the primary motor cortex. *Acta Physiol Oxf Engl*. 2017;220(2):289-299. doi:10.1111/apha.12807

29. Sherman DA, Baumeister J, Stock MS, Murray AM, Bazett-Jones DM, Norte GE. Brain activation and single-limb balance following anterior cruciate ligament reconstruction. *Clin Neurophysiol*. 2023;149:88-99. doi:10.1016/j.clinph.2023.02.175

30. Vatansever D, Menon DK, Stamatakis EA. Default mode contributions to automated information processing. *Proc Natl Acad Sci U S A*. 2017;114(48):12821-12826. doi:10.1073/pnas.1710521114

31. Smallwood J, Bernhardt BC, Leech R, Bzdok D, Jefferies E, Margulies DS. The default mode network in cognition: a topographical perspective. *Nat Rev Neurosci*. 2021;22(8):503-513. doi:10.1038/s41583-021-00474-4

32. Cassady K, Ruitenberg M, Koppelmans V, et al. Neural predictors of sensorimotor adaptation rate and savings. *Hum Brain Mapp*. 2018;39(4):1516-1531. doi:10.1002/hbm.23924

33. Wulf G. *Attention and Motor Skill Learning*. Human Kinetics; 2007.

34. Understanding motor learning stages improves skill instruction. Human Kinetics. Accessed September 17, 2024. https://us.humankinetics.com/blogs/excerpt/understanding-motor-learning-stages-improves-skill-instruction

35. Ness BM, Zimney K, Schweinle WE, Cleland JA. DUAL-TASK ASSESSMENT IMPLICATIONS FOR ANTERIOR CRUCIATE LIGAMENT INJURY: A SYSTEMATIC REVIEW. *Int J Sports Phys Ther*. 2020;15(6):840-855. doi:10.26603/ijspt20200840

36. Shi H, Ren S, Miao X, et al. The effect of cognitive loading on the lower extremity movement coordination variability in patients with anterior cruciate ligament reconstruction. *Gait Posture*. 2021;84:141-147. doi:10.1016/j.gaitpost.2020.10.028

37. Melick N van, Cingel REH van, Brooijmans F, et al. Evidence-based clinical practice update: practice guidelines for anterior cruciate ligament rehabilitation based on a systematic review and multidisciplinary consensus. *Br J Sports Med*. 2016;50(24):1506-1515. doi:10.1136/bjsports-2015-095898

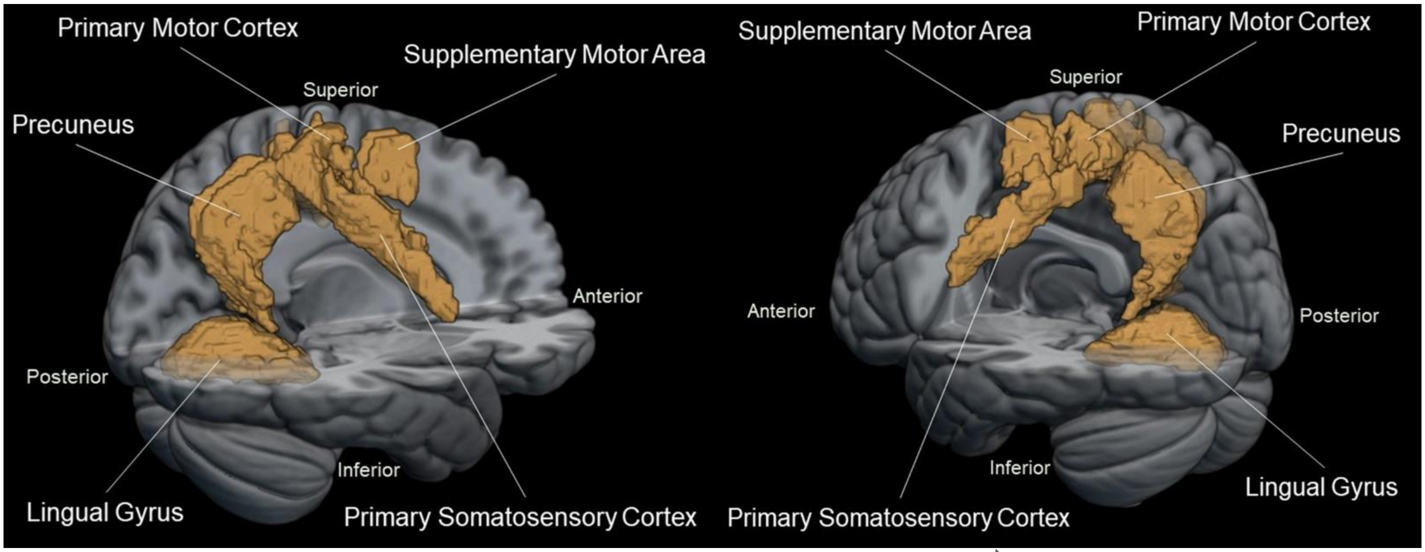

Fig. 1 Oblique, sagittal plane views of the anatomic regions of interest created to assess brain activity (percent signal change of the brain's blood oxygen level dependent response) from the move-rest contrasts to assess differences across the internal and external focus of attention conditions.

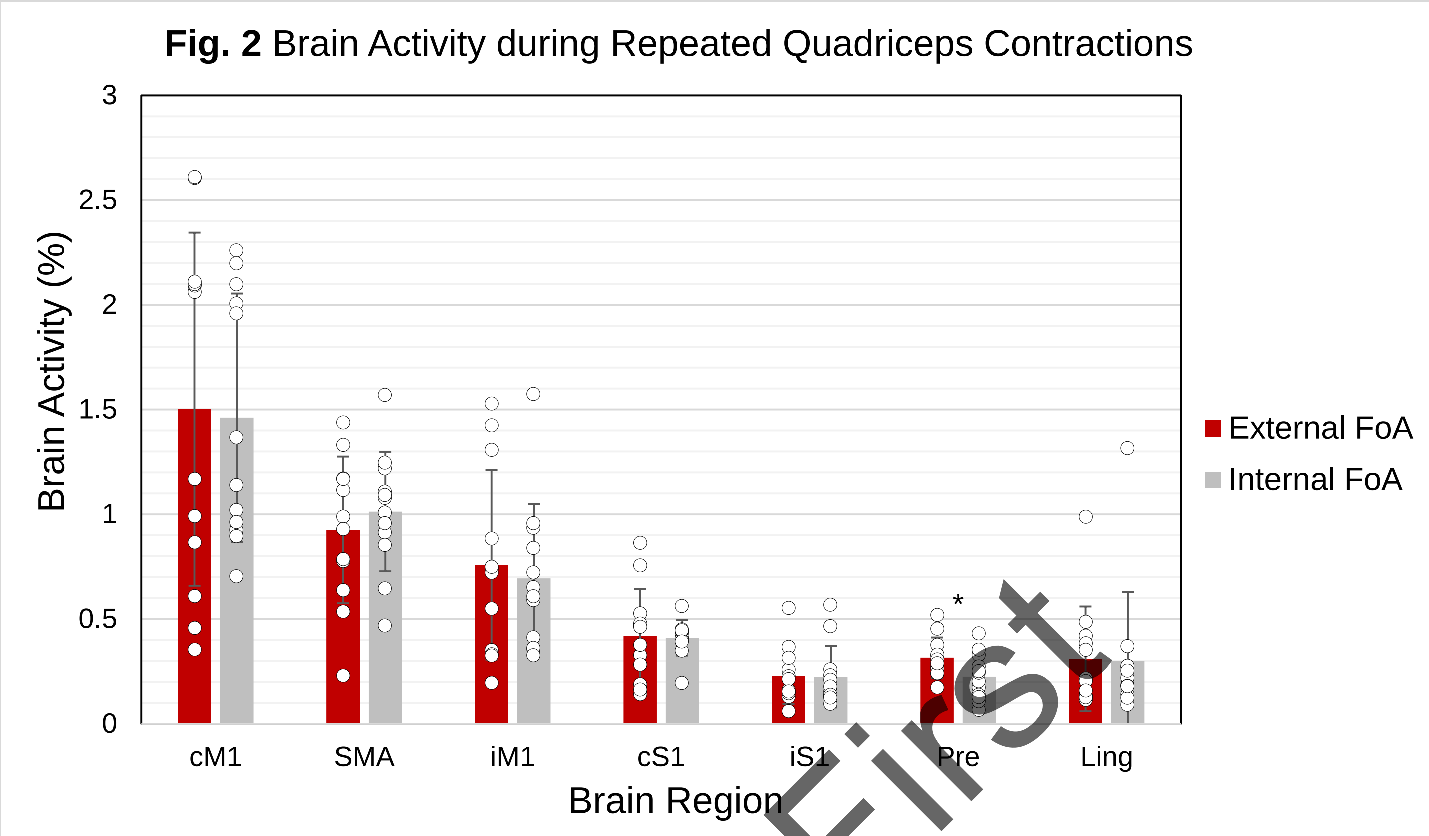

Fig. 2 Move-rest brain activity (percent signal change (Δ) of the brain's blood oxygen level dependent response) comparisons for external and internal focus of attention conditions. Statistical significance between conditions was determined using paired samples t-tests, set *a priori* at $p \leq 0.05$. * Indicates a significant difference which did not survive Bonferroni correction for multiple comparisons. cM1 = contralateral primary motor cortex, SMA = supplementary motor area, iM1 = ipsilateral primary motor cortex, cS1 = contralateral primary somatosensory cortex, iS1 = ipsilateral primary somatosensory cortex, pre = precuneus, ling = lingual gyrus.

Table 1 Percent Signal Change across FoA conditions

Brain Region	External FoA	Internal FoA	Statistics
Contralateral Motor Cortex	Δ1.50 ± 0.84%	Δ1.46 ± 0.59%	$t(11) = 0.29$, $p = 0.78$, corrected p = 1.0, $d = 0.06$
Supplementary Motor Area	Δ0.93 ± 0.35%	Δ1.01 ± 0.29%	$t(11) = 0.79$, $p = 0.45$, corrected p = 1.0, $d = 0.27$
Ipsilateral Motor Cortex	Δ0.76 ± 0.45%	Δ0.70 ± 0.35%	$t(11) = 0.57$, $p = 0.58$, corrected p = 1.0, $d = 0.16$
Contralateral S1	Δ0.42 ± 0.23%	Δ0.41 ± 0.09%	$t(11) = 0.16$, $p = 0.88$, corrected p = 1.0, $d = 0.05$
Ipsilateral S1	Δ0.23 ± 0.13%	Δ0.22 ± 0.15%	$t(11) = 0.06$, $p = 0.95$, corrected p = 1.0, $d = 0.02$
Bilateral Precuneus	Δ0.32 ± 0.10%	Δ0.23 ± 0.11%	$t(11) = 3.24$, $p = 0.008$, corrected p = 0.056, $d = 0.88$
Bilateral Lingual Gyrus	Δ0.31 ± 0.25%	Δ0.30 ± 0.33%	$t(11) = 0.19$, $p = 0.85$, corrected p = 1.0, $d = 0.03$

Table 1 Move-rest brain activity (percent signal change (Δ) of the brain's blood oxygen level dependent response) comparisons for external and internal focus of attention conditions. Two p-values are presented, the first is uncorrected for multiple comparisons, corrected p = p-value after applying Bonferroni corrections for multiple comparisons. S1 = primary somatosensory cortex, t = test statistic, and d = Cohen's d for effect sizes, interpreted as ≤0.2, 0.5, and ≥0.8 as small, medium and large respectively.

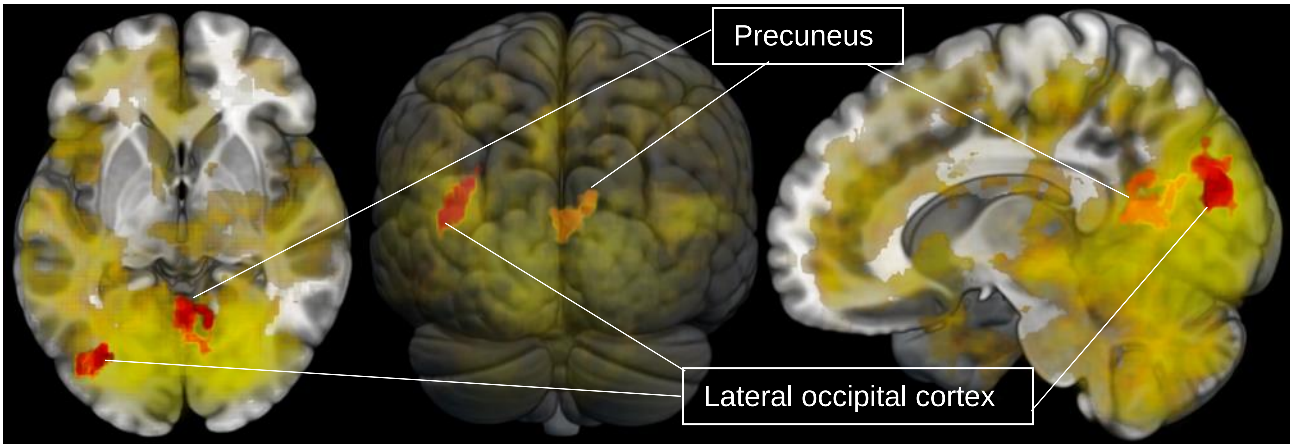

Fig. 3 Default Mode Network (DMN) intra-network connectivity analysis results. The DMN, as identified in our group level MELODIC analysis, is depicted in yellow and clusters identified as having greater intra-network connectivity in the external focus of attention condition compared to internal focus of attention are in red, indicating the regions in red demonstrated greater connectivity to the rest of DMN in the external focus condition. Images were generated in MRIcroGL and clusters thresholded at 0.95. Left image = axial view, middle image = coronal view, right image = sagittal view.