Degenerative cervical myelopathy (DCM) is a debilitating form of degenerative disc disease, affecting millions of adults older than 50 years. It is caused by progressive compressive abnormalities of the vertebral column that result in spinal cord damage due to both mechanical and biological injury. Chronic spinal cord compression causes necrosis and demyelination of gray and white matter, ultimately resulting in progressive neurological impairment and physical disability. Supraspinal alterations within the sensory and motor cortices have been demonstrated in DCM patients, commonly attributed to injury to the projecting neurons. Neural plasticity of the cortical network allows for minimization of functional impairment and occurs via synaptic modification of preexisting connections and/or the development of new circuitry. Both functional MRI (fMRI) and diffusion imaging studies have demonstrated increased functional and anatomical connectivity within the primary motor area and supplementary motor area (SMA) in DCM patients, and such reorganization is associated with worsened neurological status.

While neurological function of patients with DCM may be preserved by neural plasticity, the cerebral changes and reorganization after surgical decompression remain largely unexplored. Early intervention before manifestation of severe symptoms has frequently been advocated, predominantly based on the degree of neurological impairment and imaging features. Cessation of functional deterioration or reorganization may contribute to improved neurological function, indicating the importance of early surgical intervention.
even functional improvement after decompressive cervical surgery has been reported by several groups, where activation in primary sensorimotor cortices, including the precentral and postcentral gyri, was correlated with improvement.11–14 However, the specifics of the cerebral functional and structural changes associated with decompression remain understudied.

In the present study, we sought to further investigate the cerebral functional reorganization and any macrostructural changes that occur following decompressive surgery in DCM patients. Both high-resolution T1-weighted structural scans and resting-state fMRI scans were obtained in all subjects. Supraregional differences between DCM patients who underwent surgery and neurologically intact healthy controls (HCs) were identified. In addition, intragroup differences between DCM patients pre- and postsurgery were elucidated. We hypothesized that DCM patients undergo rapid functional changes within the brain in clinically relevant regions proportional to the degree of postoperative recovery of neurological function, but macroscopic morphological changes may be slower and therefore too subtle to be detected within 3 months of recovery.

### Methods

#### Patient Population

Nineteen DCM patients were prospectively enrolled in a cross-sectional observational study involving MRI paired with clinical assessment. All patients were recruited from an outpatient neurosurgery clinic. Exclusion criteria included 1) previous cervical spine surgery; 2) age <18 or >85 years; 3) clinical or radiological evidence of stroke or other neurological disease; 4) cardiac pacemaker or other non–MRI-compatible implant; 5) musculoskeletal, degenerative joint disease, or other medical cause of weakness or pain that affected use of the hands and gait; and 6) severe claustrophobia. All subjects signed institutional review board–approved consent forms, and all analyses were performed in compliance with the Health Insurance Portability and Accountability Act (HIPAA).

The study cohort included 14 men and 5 women, with a mean age of 55.2 years (range 41–74 years). The modified Japanese Orthopaedic Association (mJOA) score was used to evaluate neurological function.15 A cohort of 16 neurologically intact HCs with an average age of 29 years (range 20–64 years) underwent the same MRI protocol. Table 1. The operative patients underwent cervical spine MRI, brain MRI, and neurological assessment at baseline and 3 months postoperatively.

#### Presenting Symptoms

The mean duration of preoperative symptoms was 8.2 months, with a range of 1–84 months. The most common presenting symptom in the surgical cohort was paresthesia or pain in the upper extremities and was found in 18 of the 19 patients. Sixteen patients presented with deterioration of hand function, and 16 endorsed a history of neck pain. Thirteen patients complained of gait abnormalities. One patient presented with a recent change in bladder function.

#### Physical Examination

Seven patients were found to have weakness in the upper extremities on examination, and 2 had weakness in the lower extremities. Eight patients had decreased sensation in the upper extremities, and 2 had sensory changes in the lower extremities. Hyperreflexia was the most common upper motor neuron sign and was observed in 12 patients. Hoffman’s sign was the second most common long tract sign and was elicited in 10 patients. Four patients had clonus in the lower extremities, and 1 had a positive Babinski reflex.

#### Cervical Radiographic Imaging

Fifteen of the 19 patients were noted to have T2-weighted signal abnormalities within the spinal cord parenchyma. Five of the patients had ossification of the posterior longitudinal ligament. Eleven of the patients had a lordotic cervical spine, 6 had straight alignment, and 2 had a kyphotic spinal alignment.

#### Operative Treatment

The senior author (L.T.H.) performed all surgical procedures. The surgical procedure choice was predominantly influenced by the following factors: patient age, exact location and type of pathology (e.g., ossification of the posterior longitudinal ligament), spinal alignment, and number of spinal levels involved. Eight patients underwent cervical laminectomy and fusion, 7 patients underwent laminoplasty, 3 underwent an anterior cervical discectomy and fusion, and 1 had an anterior cervical corpectomy.

### Table 1. Cohort demographics for diffusion tensor imaging analysis

<table>
<thead>
<tr>
<th>Subject Population</th>
<th>No. of Subjects</th>
<th>Mean Age, yrs</th>
<th>Mean mJOA Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>HC volunteers</td>
<td>16</td>
<td>29.4 ± 11.3 (20–64)</td>
<td>18</td>
</tr>
<tr>
<td>DCM patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Preop</td>
<td>19</td>
<td>55.2 ± 9.4 (41–74)</td>
<td>14.1 ± 2.1 (10–17)</td>
</tr>
<tr>
<td>Postop</td>
<td></td>
<td>16.8 ± 1.2 (14–18)</td>
<td></td>
</tr>
</tbody>
</table>

Mean values are presented as the mean ± SD (range).
Image Preprocessing

The CONN toolbox (https://www.nitrc.org/projects/conn),\textsuperscript{16} which implements functions from the Statistic Parametric Mapping (SPM; http://www.fil.ion.ucl.ac.uk/spm/) toolbox, was used to conduct the FC analysis of the brain. All fMR images were preprocessed using the standard built-in preprocessing pipeline within CONN. Spatial smoothing of the functional data was performed using an 8-mm FWHM (full width at half maximum) gaussian kernel. To carry out denoising, the signal from the white matter, CSF, and motion parameters was regressed from the functional data. Additional signal filtering was performed using a bandpass filter of 0.008–infinity Hz, to reduce noise due to physiological effects, such as respiration and pulsation, and noise due to scanner drift.

Cortical segmentation and computation of cortical thickness and volume were performed using FreeSurfer (https://surfer.nmr.mgh.harvard.edu/fswiki)\textsuperscript{17–19} on the T1-weighted images. Processed brain surfaces were smoothed with an FWHM of 10 mm, then registered to a standard space. Age, which was predominantly linearly related to cortical thickness,\textsuperscript{19–21} was included as a covariate in analyses.

Statistical Analysis

After image preprocessing, a general linear model was implemented to identify reorganizations in cortical thickness and FC after surgical decompression. We performed two-sample t-tests to evaluate intergroup differences between DCM patients who underwent surgery and HCs. We also performed paired t-tests to evaluate intragroup changes in DCM patients pre- and postsurgery. The level of significance was set at $p < 0.05$ with age included as a covariate.

Results

Changes in Clinical Measurements After Surgery

The mean preoperative mJOA score of the DCM cohort was 14.1 (range 10–17), which significantly improved to 16.8 (range 14–18) after surgery ($p < 0.0001$; Fig. 1). Three-month postoperative cervical spine MRI demonstrated satisfactory decompression in each case, as demonstrated by reestablishment of visible CSF around the spinal cord and no evidence of residual osseous/soft tissue in contact with the spinal cord (Fig. 2).

Intergroup Differences in Cortical Thickness and FC

To study postsurgical structural and functional changes, we first compared the intergroup differences in cortical thickness and FC between HCs and the DCM patients. Generally, HCs demonstrated stronger FC between the cerebral cortex and the thalamus, hippocampus, and putamen (Fig. 3A). Specifically, the SMA and primary motor (precentral gyrus) and sensory (postcentral gyrus) areas displayed stronger FC with the putamen. Compared with the HCs, the visual network of preoperative DCM patients showed stronger FC to the left SMA, the sensorimotor system, and the bilateral insular cortices. Additionally, the cuneus showed stronger FC to the sensorimotor system and the left superior parietal lobule in the DCM patients preoperatively. Significant cortical atrophy was associated with increasing neurological deficit (Fig. 3B). In the left hemisphere, clusters were observed within the pars triangularis, the precentral gyrus, the superior temporal gyrus, and the lateral occipital gyrus. In the right hemisphere, the presence of clusters, including the caudal anterior cingulate; the superior parietal lobule; and the superior frontal, postcentral, and paracentral gyri, was positively correlated with mJOA scores.

Intragroup Changes in DCM Patients After Surgery

The FC analysis revealed postoperative cerebral reorganization in DCM patients (Fig. 4), where stronger FC was observed between the right superior frontal gyrus and the left cerebellum area 6, as well as between the left superior frontal gyrus and the left cerebellum area 10 (areas are based on the Automated Anatomical Atlas, which is included in the CONN toolbox). In contrast, FC between the left thalamus and the left cerebellum area 10, as well as between the right superior frontal gyrus and the left thalamus, showed reduced FC after surgery.
FIG. 3. Differences in FC (A) and morphology (B) between preoperative DCM patients and HCs. Red-yellow denotes stronger FC in HCs (increasing cortical thickness with increasing mJOA score), while blue–light blue denotes stronger FC in preoperative DCM patients (decreasing cortical thickness with increasing mJOA score). The position of the ROIs was displayed on midaxial slices. l = left hemisphere; MidFG = middle frontal gyrus; PreCG = precentral gyrus; PostCG = postcentral gyrus; r = right hemisphere; SFG = superior frontal gyrus; SPL = superior parietal lobule. Figure is available in color online only.
postcentral gyrus, was only statistically significant in DCM patients preoperatively. Macroscopic morphological analysis of cortical thickness did not identify any regions showing statistically significant differences between DCM patients preoperatively and postoperatively.

Finally, differences in FC of DCM patients after surgery were associated with improvement in neurological function. The region-of-interest (ROI)–to-ROI (Fig. 5) and ROI-to-voxel (Fig. 6) FC analysis provided insights into the cerebral alterations. For increasing mJOA score, the left cerebellum showed increased connectivity with the sensorimotor network, including the bilateral precentral gyri and the right postcentral gyrus. In contrast, FC within the cerebellum was negatively correlated with neurological improvement, especially within the posterior cerebellum. There was no association between changes in cortical thickness and neurological improvement after surgery. Symptom duration did not demonstrate a statistically significant correlation with FC on preoperative or postoperative fMRI within the cohort.

**Discussion**

Cortical reorganization has been shown to play an important role in preserving neurological function in DCM patients. Through neuronal plasticity, the structural and FC network adapts by either modifying preexisting connections or creating new circuitry. After surgical decompression, preservation and even recovery of motor function have been widely reported. It has been suggested that decompression of the compressed spinal cord induces cortical reorganization, and direct association between pre- and postoperative status in cortical sensorimotor activation in relation to behavioral improvement has been observed with fMRI. Bhagavatula et al. have reported postsurgical recruitment of cortical areas, such as the postcentral gyrus, premotor cortex, and supplementary cortex, which correlated with improved dexterity. Furthermore, using fMRI during a three-finger pinch task, Dong et al. found that the pinch-related activation in sensorimotor cortex contralateral to the movement paradigm, which was reduced in DCM patients, showed functional
FIG. 5. Correlation between ROI-to-ROI FC and improving neurological status (ΔmJOA) for DCM patients following surgical treatment. Yellow-red denotes increasing FC associated with increasing ΔmJOA, while blue–light blue denotes decreasing FC associated with increasing ΔmJOA. The position of the ROIs was displayed on midaxial slices. Figure is available in color online only.

FIG. 6. Brain surface display of correlation between ROI-to-voxel FC and improving neurological status (ΔmJOA) for DCM patients after surgical treatment. Seeding ROI was bilateral cerebellum areas 4–6. Yellow-red denotes increasing FC associated with increasing ΔmJOA, while blue–light blue denotes decreasing FC associated with increasing ΔmJOA. Figure is available in color online only.
gains in the upper extremity after decompression surgery that approached the activation levels of the HCs.12
In addition to task-based fMRI, several groups also identified significant cortical reorganization using resting-state fMRI.22–24 In comparison with DCM patients preoperatively, postoperatively, the patients showed increased FC between the bilateral thalamus and posterior cingulate lobe, angular gyrus, and medial prefrontal cortex, but significantly decreased FC between the bilateral thalamus, paracentral lobe, and precentral gyrus. Compared with the HCs, DCM patients showed significant differences in the visual and left sensorimotor cortices, the right superior frontal gyrus, and the right temporoparietal junction after surgical decompression. These investigations highlight the improvement and adaptations of the supraspinal functional activity and connectivity that occur after cervical decompression surgery and their potential impact on clinical recovery.

Consistent with previous findings, this study identified changes in cerebral structure and FC, supporting the hypothesis that cervical decompression can reorganize brain activity. After surgical decompression, patients postoperatively demonstrated significant neurological improvement, which was closely associated with increasing FC between the cerebellum and the pre- and postcentral gyri, but with no postoperative macroscopic morphological changes. These findings may have significant implications toward understanding the pathogenesis of DCM and recovery after surgical intervention.

Cerebral Alterations in DCM Patients Prior to Surgery

In the present study, we first conducted multiple analyses to identify cerebral alterations by comparing differences in morphology and FC between preoperative DCM patients and HCs. In addition to seeding common ROIs, we also included visual networks and cerebellum as seeds in the intergroup difference analysis. Consistent with previous studies, we proposed underlying biomarkers for disease severity and progression in patients with cervical spondylotic myelopathy,3,9 we demonstrated that DCM patients preoperatively, compared with HCs, have weaker FC from the putamen, thalamus, and hippocampus to the primary sensorimotor areas, and cortical atrophy associated with the worsened neurological impairment was seen in the caudal anterior cingulate, the superior frontal gyrus, as well as para-, pre-, and postcentral gyri.

The importance of visual cortical activity in DCM patients has been previously demonstrated,24,25 where FC alterations in DCM patients revealed differences between the visual cortex and the posterior cingulate gyrus. Consistent with those earlier studies, our results found that prior to surgery the sensorimotor network, bilateral insular cortices, and SMA each exhibited greater FC with the visual network, suggesting that patients’ greater reliance on visual inputs is a feature of their compensatory mechanism. This finding is akin to the premise of the Romberg test, which is based on the concept that standing balance requires appropriate functioning of 2 of the 3 following senses: proprioception, vestibular function, and vision. Impairment of spinal cord proprioceptive function can be unmasked by removing visual input during the test, revealing that the patient was utilizing vision to compensate for dorsal column dysfunction.26

Cerebral Changes in DCM Patients After Surgery

We found a stronger FC between the left thalamus and the left cerebellum area 10, as well as between the right superior frontal gyrus and the left postcentral gyrus, in preoperative DCM patients and increased FC between the cerebellum and the superior frontal gyrus after surgical decompression. The superior frontal gyrus is involved in self-awareness, in coordination with the action of the sensory system,27 while the thalamus plays an important role in relaying sensory and motor signals. In previous fMRI studies, we demonstrated that worsened neurological impairment in DCM patients, as measured by their mJOA scores, was associated with increased FC between the superior frontal gyrus and the primary sensorimotor regions but decreased FC from the cerebellum and thalamus to the anterior and posterior cingulate and frontal lobe regions.9 In addition, Hrabálek et al. showed that DCM patients have functional activation increases that are not limited only to the primary sensorimotor cortex but are also found in the SMA, anterior cingulate, thalamus, basal ganglia, and cerebellum.28 Consistent with these findings, FC differences observed between DCM patients from preoperatively to postoperatively indicated that compensatory inputs are actively adapted by DCM patients to preserve neurological function prior to surgery, and ongoing functional reorganization is associated with effective postoperative recovery.

The mean mJOA score showed significant improvement of 2.7 after surgical decompression, and such improvement was closely correlated with increased FC between cerebellum and the pre- and postcentral gyrus. In particular, the ROI-to-voxel analyses identified that the activated regions within the pre- and postcentral gyrus represent the arm, elbow, and hand, suggesting improvement in postural control and alleviated symptoms such as the weakness in the muscles of arms and hands after successful surgical decompression.12 The corticospinal tract plays an important role in voluntary motor control and modulating sensory information.29 Previous studies have shown that DCM patients experience white matter tract damage to the bilateral corticospinal tracts, with a significantly reduced number of streamlines compared with HCs.20

Compared with the corticospinal tract, the cerebellum has been relatively understudied in DCM patients, yet it is critical for coordination of voluntary movements such as ambulation and hand dexterity, both of which are commonly impaired in DCM patients. Prior to surgery, our results showed that HCs demonstrated stronger FC between the cerebellum and the pre- and postcentral gyri when compared with preoperative DCM patients, and, after surgical decompression, increased FC between the subregions of the cerebellum and the primary sensorimotor areas was observed in postoperative DCM patients. This recovery in FC between the cerebellum and pre- and postcentral gyri, which correlates with improvement in mJOA score, further highlights the beneficial effect of decompression surgery on sensorimotor function.
Limitations
Analyses based on morphology and connectivity have been used in our previous studies to demonstrate cortical reorganization of the sensorimotor system to compensate for potential functional loss due to progressive spinal cord injury. The current study investigated the cerebral neural plasticity of DCM patients undergoing surgical decompression. To account for the mean age of our HC cohort being significantly lower than that of the DCM cohort, all of our analyses, including the t-test, paired t-test, and correlation analysis, have controlled for the ages of both cohorts as a covariate. Additionally, there was some value of including this particular HC cohort, as it provided a standard for optimal FC with which the surgical cohort could be contrasted. Although our results provide evidence on how surgical decompression can alter FC, a longitudinal follow-up study is necessary to track continued morphological and structural changes. It is likely that further plasticity may evolve over time secondary to activity-dependent mechanisms related to motor practice and learning. Validation from diffusion-weighted imaging could help to confirm the reorganization of such FC, as well as the formation of new connections in DCM patients who have exhausted their compensatory mechanism of recruitment and reorganization.

Conclusions
Reorganization in FC between the cerebellum and primary sensorimotor regions was associated with significant neurological improvement after successful surgical decompression. However, no macroscopic morphological changes were observed in postoperative DCM patients compared with preoperative DCM patients.

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References


**Disclosures**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**Author Contributions**

Conception and design: Holly, Ellingson. Acquisition of data: Holly, Wang, Ellingson, Islam, Laiwalla. Analysis and interpretation of data: Holly, Wang, Ellingson, Salamon. Drafting the article: Holly, Wang, Ellingson, Laiwalla, Salamon. Critically revising the article: Holly, Ellingson. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Holly. Statistical analysis: Wang, Ellingson. Administrative/technical/material support: Holly, Ellingson. Study supervision: Holly, Ellingson.

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