Anatomical and Functional Enhancements of the Insula after Loss of Large Primary Somatosensory Fibers

Marta Čeko1,5, David A. Seminowicz1,2,7, M. Catherine Bushnell1,2,3,4 and Hakan W. Olausson6

1Alan Edwards Centre for Research on Pain, 2Faculty of Dentistry, 3Department of Anesthesiology, 4Department of Neurology and Neurosurgery, Faculty of Medicine and 5Integrated Program in Neuroscience, McGill University, Montreal, QC, Canada H3A 2T5 6Department of Clinical Neurophysiology, Sahlgrenska University Hospital, S-413 45 Gothenburg, Sweden and 7Department of Neural and Pain Sciences, University of Maryland School of Dentistry, Baltimore, MD 21201, USA

Address correspondence to Marta Čeko, Alan Edwards Centre for Research on Pain, 3640 University St., Rm M/19, Montreal, QC, Canada H2A 3B3. Email: marta.ceko@mail.mcgill.ca

Brain changes associated with the loss of a sensory modality such as vision and audition have previously been reported. Here, we examined the effect of loss of discriminative touch and proprioception on cortical thickness and functional connectivity. We performed structural magnetic resonance imaging and resting-state functional magnetic resonance imaging scans on a 60-year-old female who at age 31 suffered a selective loss of large-diameter myelinated primary afferents and, therefore, relies mainly on her intact thin-fiber senses (temperature, pain, itch, and C-fiber touch) and vision to negotiate her environment. The patient showed widespread cortical thinning compared with 12 age-matched female controls. In contrast, her right anterior insula was significantly thick. Seed-based resting-state analysis revealed that her right anterior insula had increased connectivity to bilateral posterior insula. A separate independent component analysis revealed the increased connectivity between the insula and visual cortex in the patient. As the insula is an important processing area for temperature and C-fiber tactile information, the increased intrainsular and insular-visual functional connectivity could be related to the patient’s use of C-fiber (gentle) touch and temperature information in conjunction with visual information to navigate her environment. We, thus, demonstrated plasticity in networks involving the insular cortex following denervation of large-diameter somatosensory afferents.

Keywords: cortical thickness, functional MRI, gray matter, pain, plasticity, resting-state connectivity

Introduction
Individually who have lost the use of a sensory modality, such as sight or hearing, must utilize the remaining sensory modalities to a greater degree and develop other compensatory mechanisms to function in the world. Several studies now show that such compensation can be attended by morphological changes in the brain, with regions involved in the compensatory mechanisms showing hypertrophy. For example, deaf individuals who have learned sign language show hypertrophy in the left motor hand cortex (Penhune et al. 2003). Similarly, deaf subjects show more gray matter (GM) in the left posterior insula, which was interpreted to be related to lip-reading and articulatory-based (rather than auditory-based) representations of speech for deaf individuals (Allen et al. 2008). In terms of white matter (WM) tracts, deaf people show increases in diffusion anisotropy in the forceps major of the corpus callosum, where interhemispheric connections between visual cortices exist (Kim et al. 2009). Similarly, blind individuals show widespread hypertrophy outside the occipital lobes, particularly in frontal and prefrontal regions (Lepore et al. 2010) and subjects with vestibular failure show increased GM in parts of the visual and somatosensory cortices, hypothesized to be related to an increased importance of visual motion processing and the use of proprioceptive information to compensate for vestibular dysfunction (Zu Eulenburg et al. 2010).

We have previously studied a unique patient who sustained a selective deafferentation of large-diameter myelinated sensory fibers (sensory ganglionopathy), with sparing of most small-diameter primary afferent fibers that transmit temperature, pain, and C-tactile information (Cooke et al. 1985; Olausson et al. 2002; Cole et al. 2006; Bjorsmdotter et al. 2009). The patient lacks discriminative touch and proprioception, so she relies mainly on temperature information when her skin touches a surface, as well as vision, to navigate her environment. Some C-fibers respond to touch, but mainly to slow stroking, and these fibers are present only on hairy skin (Cole et al. 2006). The patient can discern the presence of such stroking, although she has only a crude ability to localize the skin contact (Olausson et al. 2008). Functional neuroimaging studies show activation in the patient’s insular cortex during slow stroking of the hairy skin (Olausson et al. 2002; Bjornsmdotter et al. 2009). Evidence from functional neuroimaging studies in healthy subjects shows that the insula is an important cortical processing area for C-fiber information (Olausson et al. 2002, 2005; Craig 2009). Thus, we hypothesized that because of the patient’s compensatory use of C-fiber–based information, the insular cortex would show an anatomical and functional enhancement.

Methods
Subjects
We included 12 neurologically intact right-handed female controls (age 45–63, mean 55.8, standard deviation [SD] 6.1) and a deafferented patient, G.L. (right-handed female, age 60). At age 31, G.L. suffered polyradiculitis, leading to a specific and permanent loss of large myelinated (Aβ) afferents below the level of the nose (sensory ganglionopathy). A sural nerve biopsy showed a complete reduction of large-diameter myelinated fibers, whereas small-diameter myelinated fibers were largely unaffected (Cooke et al. 1985; Forget and Lamarre 1995); for more details about G.L., see http://deafferented.apinc.org. Consequently, G.L. has no sense of discriminative touch and proprioception below the level of the nose. Informed consent was obtained from all subjects, and the procedures were approved by the McGill Internal Review Board.
General Procedures
All subjects participated in one magnetic resonance imaging (MRI) scanning session, which included an anatomical as well as a functional scan. During the functional scan, the subjects were instructed to lie calmly with their eyes fixated on a crosshair in the middle of the screen, not thinking about or concentrating on anything in particular. Throughout the session, the participants wore earplugs to protect them from the scanner noise, and their heads were immobilized.

Data Acquisition
Each participant was scanned on a Siemens Trio 3T MRI system with a standard 8-channel head coil. The anatomical MRI scan (duration 10 min) was acquired using a 3D-magnetization-prepared rapid acquisition by gradient echo $T_1$-weighted sequence. The protocol had an inversion time of 900 ms, flip angle of 9°, echo time (TE) of 2.98 ms, and repetition time (TR) of 2300 ms. The images had an isotropic resolution of 1 mm and field of view of 256 mm.

The functional MRI scan was collected using a blood oxygenation level-dependent (BOLD) protocol with a $T_2$-weighted gradient echo planar imaging sequence with TE of 30 ms and TR of 2260 ms, and 38 slices with an isotropic resolution of 3.5 mm. Axial slices were oriented 30° from the line between the anterior and posterior commisures, covering the entire brain, and excluding the eyes. After discarding the first 3 volumes to allow for signal equilibration, we acquired 128 volumes, for a total scan time of about 5 min. In G.L., we performed 2 resting-state runs.

Anatomical MRI Analysis

Data Preprocessing
For cortical thickness analysis, data from the patient and all 12 control subjects were preprocessed using the CIVET pipeline (v. 1.1.9) (Zijdenbos et al. 2002; Ad-Dabagh et al. 2006; Fahim et al. 2010). In brief, the steps included nonuniformity correction for field inhomogeneity (Sled et al. 1998), normalization (both nonlinear and linear) to the MNI/ICBM 152 template (Collins et al. 1994, 1995), tissue classification (labeling each voxel as GM, WM, or cerebrospinal fluid (CSF)), and partial volume estimation (Tohka et al. 2004), which labels voxels as partially GM, WM, and/or CSF (e.g., a voxel covering the pial boundary could be labeled 50% GM and 50% CSF). A cortical fitting stage registered the brain surfaces to a model that calculates 81 labels voxels as partially GM, WM, and/or CSF (e.g., a voxel covering the pial boundary could be labeled 50% GM and 50% CSF). A cortical fitting stage registered the brain surfaces to a model that calculates 81
cortical thickness values.

Cortical Thickness Analysis
SurfStat (http://www.math.mcgill.ca/keith/surfstat/) was used to read in the preprocessed data and display cortical thickness maps. To compare a single subject (G.L.) to a group, we computed SD maps of cortical thickness in the healthy controls and report whether cortical thickness values in G.L. were above or below 2.5 SDs from the control mean (i.e., 99% confidence interval), indicating deviation from the normal cortical thickness values. Thus, the following contrasts were calculated:

$$ [G.L. > \text{controls}] = [\text{mean}_{\text{controls}} + 2.5 \text{SD}_{\text{controls}}] - \text{G.L.}, $$

and controls $>$ G.L. = [mean$_{\text{controls}}$] $-$ [mean$_{\text{controls}} + 2.5 \text{SD}_{\text{controls}}$] $-$ G.L.). To further describe the extent of deviation from the normal score, we compared cortical thickness value at peak (location of maximum difference) between G.L. and healthy controls with the modified two-tailed $t$-test, designed specifically to compare a single individual’s data point against norms derived from small samples (Crawford et al. 1998; Crawford and Garthwaite 2002). This statistical approach was used in all consequent analyses.

Resting-State Functional MRI Data
Data from one control subject (54 years old) had to be discarded due to imaging artifacts. The resting-state functional MRI scans of the patient and 11 controls subjects were processed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/). Briefly, preprocessing involved a 6-parameter rigid body correction for head motion, co-registration to the $T_1$-weighted anatomical image, and normalization to the MNI/ICBM 152 template, followed by smoothing with an 8-mm Gaussian kernel. Next, we band-pass filtered (0.009 Hz < f < 0.08 Hz) the data using the neuroimaging analysis kit (NIAK) toolbox (http://code.google.com/p/niak/) to reduce the effect of low-frequency drift and high-frequency noise. We conducted 2 types of resting-state analysis, seed-based and independent component analysis (ICA).

Seed-Based Functional Connectivity
We used the MarsBar toolbox for SPM8 (http://marsbar.sourceforge.net/) (Brett et al. 2002) to extract time-course data from the preprocessed functional scans of each subject. The selected seed was chosen based on the results of the cortical thickness analysis that identified a region in the right anterior insula that was thicker in the patient than controls. The region of interest (ROI) was a sphere (3 mm radius) centered on the peak voxel in that region (Fig. 1). For each subject, the time-course data from the average signal of all voxels in the ROI was then used as the independent variable in a whole-brain linear regression. To control for non-neuronal noise, we included as nuisance variables 6 parameters derived from head motion correction, and 7 further parameters, representing the time-course data from 3 ventricular ROIs and 4 WM ROIs. We chose not to remove the average whole-brain signal since such a correction might introduce artificial anticoncorrelations (Fox et al. 2009). We created correlation maps across the whole brain for each subject and then computed contrasts between the patients and controls ± 2.5 SD as described above. The peak differences between G.L. and controls were further described with the modified $t$-test as described above (Crawford et al. 1998; Crawford and Garthwaite 2002).

Independent Component Analysis
In addition to the seed-based functional connectivity analysis, we performed an ICA of the insular network (Damoiseaux et al. 2006; Seeley et al. 2007; Taylor et al. 2009), using the default settings of the Group ICA of functional magnetic resonance imaging (fMRI) (GIFT) toolbox for SPM8 (http://icatb.sourceforge.net/groupica.html; Calhoun et al. 2001). We performed ICA on the group data (Infomax algorithm), combining all subjects’ data in the temporal domain and extracting common spatial components and extracting 30 components. The resultant components were then back-projected for each subject, so that each subject had a component map. We then computed comparison maps between the patient and controls ± 2.5 SD as described above. Modified $t$-tests were performed on the peak differences as described above (Crawford et al. 1998; Crawford and Garthwaite 2002).

Results
Cortical Thickness Analysis
The deafferented subject G.L.’s cortex was significantly thinner with healthy controls in large parts of frontal, temporal, and parietal cortices (Fig. 1A, B and Table 1). Primary somatosensory cortex (S1) was significantly thinner on the left, with a similar trend on the right side (Fig. 1C, Table 1, and Supplementary Fig. 1). Despite these widespread regions of thinner cortex, the patient had significantly thicker insular and cingulate cortices, with the largest difference observed in the right anterior insula (aINS) (Fig. 1A, B and Table 1). Indeed, the patient’s right aINS was thicker than that of any control subject (Fig. 1C). Despite the regional differences between the patient and control subjects, the total GM, WM, and CSF volume did not differ significantly between G.L. and controls (Fig. 1D).
Figure 1. Altered cortical thickness with preserved brain GM, WM, and CSF volumes. (A) left panel, restricted cortical thickening of the right anterior insula and left cingulate regions in G.L. compared with 12 age-matched female controls [yellow, G.L.>(controls + 2 SD); red, G.L.>(controls + 2.5 SD)]; right panel, widespread cortical thinning in G.L. [light blue, (controls − 2 SD)>G.L.; dark blue, (controls − 2.5 SD)>G.L]. Displayed on the group average brain, left side of the brain is on the left. (B) Cortical thickness maps for G.L. (left panel) and healthy controls (right panel). Arrows on G.L.'s map are pointing to the left S1 (white arrow; area of thinnest cortex) and right anterior insula (black arrow; area of thickest cortex). Displayed on the group average brain, left side of the brain is on the left, color bar shows cortical thickness in mm. (C) Cortical thickness of right anterior insula (at location of thickest cortex) and left S1 (at location of thinnest cortex) plotted against controls and by age. Full circle, G.L., open circles, controls; error bars represent 99% confidence intervals (2.5 SD). (D) Brain CSF, GM, and WM total volumes in G.L. and controls; n.s., not significant.

Table 1

<table>
<thead>
<tr>
<th>Brain region</th>
<th>MNI coordinates (mm)</th>
<th>Cortical thickness (mm)</th>
<th>T value at peak</th>
<th>P value at peak</th>
<th>Cluster size (voxels)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls &gt; G.L.</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>L S1</td>
<td>−9, −33, 71</td>
<td>2.21 (0.18)</td>
<td>1.76</td>
<td>0.73</td>
<td>−7.80</td>
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<tr>
<td>R S1 (contralateral to L S1 peak)</td>
<td>11, −33, 74</td>
<td>2.24 (0.16)</td>
<td>1.82</td>
<td>0.70</td>
<td>−7.29</td>
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<tr>
<td>L temporal pole</td>
<td>30, −16, −42</td>
<td>3.03 (0.11)</td>
<td>3.35</td>
<td>2.57</td>
<td>−7.80</td>
</tr>
<tr>
<td>R temporal pole</td>
<td>−52, −14, −13</td>
<td>3.37 (0.14)</td>
<td>3.01</td>
<td>2.77</td>
<td>−6.77</td>
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<tr>
<td>L parietal</td>
<td>−58, −50, −8</td>
<td>2.91 (0.11)</td>
<td>2.64</td>
<td>2.17</td>
<td>−7.64</td>
</tr>
<tr>
<td>R parietal (BA 39)</td>
<td>46, −75, 32</td>
<td>3.01 (0.11)</td>
<td>2.73</td>
<td>2.17</td>
<td>−7.26</td>
</tr>
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<td>L DLPFC (BA 22)</td>
<td>−30, 18, −42</td>
<td>2.97 (0.13)</td>
<td>2.71</td>
<td>2.29</td>
<td>−6.55</td>
</tr>
<tr>
<td>R premotor</td>
<td>34, −4, 52</td>
<td>2.91 (0.15)</td>
<td>2.62</td>
<td>2.16</td>
<td>−6.23</td>
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<td>G.L. &gt; controls</td>
<td></td>
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<td>R anterior insula</td>
<td>40, 3, −13</td>
<td>3.86 (0.23)</td>
<td>4.43</td>
<td>4.03</td>
<td>3.91</td>
</tr>
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<td>L ACC</td>
<td>−2, −43, 11</td>
<td>2.80 (0.18)</td>
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<td>3.45</td>
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<td>L subgenual ACC</td>
<td>−4, 17, −8</td>
<td>2.57 (0.22)</td>
<td>3.12</td>
<td>3.23</td>
<td>3.20</td>
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<tr>
<td>L posterior MCC</td>
<td>−2, 0, 31</td>
<td>2.68 (0.17)</td>
<td>3.10</td>
<td>3.22</td>
<td>3.11</td>
</tr>
</tbody>
</table>

Note: BA, Brodmann area; DLPFC, dorsolateral prefrontal cortex; ACC, anterior cingulate cortex; MCC, midcingulate cortex; L, left; R, right.

*Mean for control + 2.5 SD (for G.L. > control) and −2.5 SD (for control > G.L.)

*As derived from Crawford’s modified t-test performed on cortical thickness (mm) at peak (i.e., coordinates of greatest difference between G.L. and healthy controls). Underlined values (G.L.) are 3 SD (99.9% confidence interval) outside the controls’ mean.

*Number of voxels for the controls > G.L. contrast not shown, since the peaks are part of a contiguous cluster covering much of the brain surface.
Seed-Based Functional Connectivity Analysis

The results from G.L.’s 2 functional runs were nearly identical, and therefore, we used the average over the 2 scans for the analysis. Employing a seed-based analysis with the ROI on the right aINS, the region where G.L. had the thickest cortex compared with control subjects, we found that her right aINS had stronger functional connectivity with the right temporal pole and within right and left mid/posterior parts of the insula (Fig. 2C and Table 2).

In contrast, her right aINS had weaker functional connectivity with parts of the temporal lobes and cerebellum than observed in controls (Fig. 2D, Table 2, and Supplementary Table 1).

ICA-Based Functional Connectivity

To support the seed-based connectivity results, we performed a model-free analysis (ICA) of insular resting-state connectivity. The results of this analysis confirmed those derived from the seed-based functional connectivity analysis, in that G.L. had increased connectivity to several areas within insula. She also had increased functional connectivity of the insula with the visual cortex and left S1 (Fig. 2C, Table 2, and Supplementary Table 1). In contrast, G.L. had decreased connectivity of the insula with parts of the parietal and temporal lobe, cingulate cortex and with cerebellum (Fig. 2D, Table 2, and Supplementary Table 1).

Discussion

We have demonstrated structural and functional abnormalities of the brain of an individual who sustained the loss of large myelinated primary afferent fibers in adult life. Compared with healthy controls, the patient’s cortex was mostly thinner, including some of the somatosensory cortices. Despite these large regions of cortical thinning, parts of the patient’s insular and cingulate cortices were significantly thicker than in controls. Resting-state functional imaging revealed an increased intrainsular connectivity, as well as an increased insular-visual cortical connectivity, suggesting an adaptive plasticity as a compensation for large-fiber afferent somatosensory denervation.

Gray Matter Increases in Regions Involved in Small Fiber Function

Despite the widespread cortical thinning, the patient in our study had regions of thicker cortex in the cingulate and insula. These increases could be interpreted as hypertrophy in brain regions involved in compensatory mechanisms used.

Figure 2. Resting-state functional connectivity of the right insula. (A) left panel, seed correlation map for G.L.; right panel, ICA component map for G.L.; color bar shows contrast values (a.u.). (B) left panel, average seed correlation map of 11 controls; right panel, ICA average component map of 11 controls, color bar shows contrast values (a.u.). (C) left panel, seed-based connectivity contrast map G.L. > controls + 2 SD (red); right panel, ICA-based connectivity contrast map G.L. > controls + 2 SD (red). (D) left panel, seed-based resting-state connectivity contrast map controls − 2 SD > G.L. (blue); right panel, ICA-based connectivity contrast map controls − 2 SD > G.L. (blue). Maps are displayed on the MNI/ICBM 152 template, left side of the brain is on the left. Maps showing G.L.’s scores outside 2 SD of the controls’ mean are used for visualization, whereas only scores outside 2.5 SD of the controls’ means are considered to be statistically significant (cf. Table 2).
Within the insula: seed-based analysis and ICA as a data-driven approach to strengthen and complement these findings. Seed-based and ICA-based functional connectivity are conceptually different measures producing similar, but not identical results (Van Dijk et al. 2010; Joel et al. 2011). Both methods explore inter-regional synchrony of low-frequency BOLD fluctuations. Seed-based analysis temporally correlates a specified seed region of interest with all other voxels in the brain, while ICA decomposes the data into spatially independent networks. Using a seed-based approach, we could detect the functional connectivity of an ROI in the anterior insula with several regions across the brain; however, this did not tell us if those regions were part of the same intrinsic network. To this end, we used the ICA, which confirmed that the anterior insula seed and its functionally connected regions indeed belonged to the intrinsic insular network.

Both the seed-based and ICA connectivity analyses revealed increased intrainsular connectivity, both between left and right insulae and between right anterior and more posterior regions. We speculate that the increased intrainsular connectivity is related to the patient’s increased use of thermal stimuli, because other studies have shown that the physical stimulus intensity of thermal stimuli are coded in the posterior insula, whereas the perceived intensity is coded in the right aINS. This dissociated localization of the coding of physical and perceptual properties of thermal stimuli suggests that there are important intrainsular connections linking these regions, which could be strengthened with use in our patient.

In addition, the examination of the insula network revealed an increased functional connectivity between the insula and visual cortex in the deafened patient. This is consistent
with functional neuroimaging studies showing that the insula is activated during tasks involving cross-modal integration of tactile and visual information (Hadjikhani et al. 1998; Banati et al. 2000). Along with her increased use of thermal information to compensate for lack of proprioception, the patient in our study reports using visual information as much as possible to know the position of her limbs, including keeping her environment lit day and night. Such compensatory behavior could strengthen the visual-insular integration.

In addition to thermal processing in the insular cortex, there is evidence that the input from unmyelinated C-fiber tactile responsive primary afferents is processed in the insula and that this input is intact in our patient (Olausson et al. 2002; Bjornsdotter et al. 2009). In fact, G.L. is unique in that she can perceive pure C-tactile stimulation (Olausson et al. 2002), and this could be related to the increased thickness and functional connectivity of the insula. Healthy subjects cannot perceive pure C-tactile stimulation, as they lose all sensation of touch when their myelinated afferents are blocked (MacKenzie et al. 1975). Consistent with G.L.’s unique perceptual capacity, she has an enhanced and more widespread fMRI activation of insular cortex to tactile stimulation compared with controls (Olausson et al. 2002), and C-tactile insular processing could also be involved in visual-tactile integration (Morrison et al. 2011).

Though increased thickness of the insula is indicative of increased afferent input (C-fibers), it could also partly be due to increased use of visual input and the heightened functional connectivity between the insula and visual cortex. Increased reliance on both C-afferent and visual information have been described in the patient (Fleury et al. 1995; Cole and Paillard 1998), and it might not be possible to discriminate which is more involved. Future work could use different combinations of visual and tactile stimulation to try to dissociate these effects.

Widespread Decreases in Cortical Thickness

Although the patient did not have significantly less total GM than control subjects, large regions of her cortex were thinner than those of controls. Primary somatosensory (S1) cortex was significantly thinner on the left, with a similar trend on the right. In fact, the patient had cortical thinning compared with all controls (except for one control in one region) across multiple regions of left and right S1 approximating different somatotopic representations (see Supplementary Fig. 1). This is perhaps not surprising, given that a prominent cortical target of pathways involving large-diameter somatosensory afferents is S1. The loss of afferent sensory drive from a specific body region in an adult is followed by functional reorganization of S1, so that the deprived S1 region is activated by sensory stimulation of the surrounding intact body regions (Merzenich et al. 1984; Pons et al. 1991; Flor et al. 1995). Despite this reorganization, there is still GM volume loss in S1 regions representing the deafferented body region (Henderson et al. 2011). The patient’s reduced GM in other cortical regions has a less obvious explanation but could be related to the more restricted life the patient has lived for the last 30 years. The patient has retained motor function in her limbs, but has no proprioceptive input below the level of the nose, and therefore requires constant visual vigilance for every purposeful movement, including walking (Cole and Paillard 1998). She had early on decided not to make an effort at walking, and had since been using a wheel chair instead (Cole and Paillard 1998). Thus, her mobility and the ability to engage in many normal activities have been greatly reduced. Widespread cortical atrophy has been observed in other disorders associated with reduced mobility, such as spinal cord injury (Wrigley et al. 2009) and amyotrophic lateral sclerosis (Grosskreutz et al. 2006; Cosottini et al. 2012).

Limitations

A major limitation of the study is that it is based on the differences between controls and a single patient. However, because of the rareness of the condition in which all large diameter somatosensory fibers are lost, attaining a group of patients would be impossible. The other patient (I.W.) with this rare disorder who we have previously tested is no longer willing to enter an MRI scanner.

Another limitation—as in all studies of cortical thickness or GM volume—is that the mechanisms underlying decreased cortical thickness are not clear. There are now many studies showing use-dependent GM increases in humans. Most of these studies involve individuals with specific training, such as musicians (Schneider et al. 2002; Gaser and Schlaug 2003; Abdul-Kareem et al. 2011), meditators (Lazar et al. 2005; Grant et al. 2010; Holzel et al. 2011), jugglers (Draganski et al. 2004), or taxi-drivers (Maguire et al. 2000). For the cross-sectional studies, the results could be interpreted as pre-existing anatomical differences that could predispose an individual to excel at an endeavor. However, longitudinal studies now show rapid morphological changes associated with only days or weeks of practicing a discipline (Draganski et al. 2004; Holzel et al. 2011). The increased GM could be due to many possible factors, including neural or glial cell genesis, increased cell size or spine density, or even changes in blood flow or interstitial fluid (May et al. 2007). The rapid changes in GM volume observed in some studies suggest the involvement of a rapidly adjusting system, such as dendritic spine or synapse turnover (Trachtenberg et al. 2002), and the induction of long-term synaptic potentiation is associated with the enlargement of the dendritic spines (Bosch and Hayashi 2011).

Conclusion

The brain is capable of rewiring in response to environmental demands, as has been seen in blindness and deafness. We have shown that in a patient lacking large diameter fibers that mediate the sense of touch and proprioception, the anterior insula cortex is thicker and the resting-state connectivity within the insula and between insula and primary visual cortex is increased. This plasticity in networks involving sensory processing and internal awareness likely reflects the brain’s adaptation to the loss of a sensory modality, allowing for enhanced multisensory integration.

Supplementary Material

Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.
Funding
This study was supported by the Swedish Research Council, the Wallenberg Foundation, and the Canadian Institutes of Health Research.

Notes
We thank Marianne and Marcus Wallenberg’s foundation for financial support (H.O.), and the team at the McConnell Brain Imaging Centre of the Montreal Neurological Institute for expert MRI data acquisition. Conflict of Interest: None declared.

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