Supplementary methods

Assessment of thermal pain threshold

The pain thresholds were assessed in the laboratory outside the MRI scanner. Quantitative sensory tests were performed with a thermal sensory analyzer (WinTSA, Medoc), using a 9 cm² contact thermode. Thermal pain thresholds were determined by an ascending method of limits, as previously described. The 9 cm² contact thermode (TSA-2001, Medoc) was placed on the palm of each hand, one at a time. The temperature was increased at a rate of 0.5 °C per second (baseline [minimal] temperature 32.0 °C, maximal temperature 53.0 °C). To determine thermal pain thresholds, participants were asked to follow the written instruction, “When thermal perception becomes painful, press the stop button immediately.” The investigation started with 3 learning trials and continued with 5 consecutive tests.

Functional data analysis

For image processing and statistical analyses, we used the SPM8 software. The procedure for data preprocessing was comparable that used in to our previous studies. The preprocessing included slice timing correction, 3-dimensional motion correction, within-subjects registration between functional and anatomical images, segmentation of the coregistered anatomical images and spatial normalization using parameters estimated during the segmentation process. The data were smoothed using a 10 mm full-width at half-maximum (FWHM) Gaussian filter, and a temporal high-pass filter of 128 s was applied. We focused our statistical analysis on the comparison contrasting the painful thermal stimulation at 45°C versus non-painful 37°C condition in the first level analysis. These single-subject contrasts were then submitted to the second level group analyses, in which we tested for potential group differences.

Voxel-based morphometry

The T₁-weighted images were corrected for bias-field inhomogeneities; registered using a linear (12-parameter affine) and a nonlinear transformation; stripped of nonbrain tissue; and classified into grey matter, white matter, or cerebrospinal fluid. A high-dimensional normalization was performed using the DARTEL template in the Montreal Neurological Institute (MNI) space that is provided with the VBM8 toolbox. Individual grey matter volume images were multiplied voxel-wise by the determinants of Jacobian matrices from nonlinear transformations before statistical analysis on local grey matter volumes was performed. Gaussian smoothing was
performed with an 8 mm FWHM kernel. The choice of this kernel was based on the study by Shen and Sterr.4
Only voxels with absolute grey matter values above 0.25 were entered into the analysis to avoid possible edge effects around the border between grey and white matter.

Cortical thickness
For the computation of the cortical thickness we used the processing stream, as implemented in FreeSurfer version 5.3.0. It includes removal of nonbrain tissue, transformation to the MNI space and segmentation of grey/white matter tissue. White and grey matter boundary is tessellated and topological defects are automatically corrected. After intensity normalization, transition of grey/white matter and pial boundary are indicated by identifying the greatest shift in intensity through surface deformation. The entire cortex of each participant was then visually inspected, and the data for those with inaccuracies in segmentation were discarded (1 healthy control). Cortical thickness was computed by finding the shortest distance between a given point on the estimated pial surface and the grey/white matter boundary and vice versa and averaging these 2 values.5
Individual native surfaces of cortical thickness were mapped onto the common FreeSurfer’s fsaverage surface using a spherical-based algorithm. Maps were smoothed using a 10 mm Gaussian kernel. The choice of this kernel was based on the study by Bernal-Rusiel and colleagues.5

References