Supplementary information

Data acquisition

Native T1-weighted structural images were acquired for all subjects on the same head-only 3T machine (SIEMENS SKYRA, Munich, Germany, 32-channel receive-only phase-array head coil). For ET patients, data was collected both at baseline and one year after thalamotomy. The acquisition parameters were as follows: TR/TE=2300/2.98 ms, isotropic voxels of 1 mm^3, 160 slices. Scanning was performed in a drug-naïve state (drugs having been stopped at least 3 days beforehand). One year after thalamotomy, the scan included a sequence with Gadolinium injection, to help better distinguish and delineate the corresponding MR signature and its volume (see below).

RS fMRI scans were acquired for the same subjects (both before and after thalamotomy for ET patients), using the same machine and the following parameters: TR/TE=3300/30 ms, flip angle=90°, voxel size 4 mm^3, 300 volumes acquired per ET patient (210 for HCs), 46 interleaved axial slices. Participants were asked to relax with their eyes closed, without falling asleep or engaging in cognitive or motor tasks.

Extraction of morphometric features

Following linear registration to Montreal Neurological Institute space and bias field removal, the image at hand was skull-stripped,[1] and voxels were classified as belonging to white matter or to another tissue category based on intensity and direct neighborhood. Following the separation of hemispheres and the removal of the cerebellum and subcortex, the interface between the white and gray matters and the pial surface were located. Local estimates of CT,

SA and MC were then extracted.[2] These voxel-wise measurements were eventually converted into P_{cort} regional values per morphometric measure, using the Desikan-Killiany atlas.[3] For each cortical brain region, a three-dimensional data point was thus obtained per subject.

Preprocessing of morphometric features

For each region, each morphometric feature (CT, SA or MC for cortical areas and volume for non-cortical ones) was modelled as:

$$M_{i,s} = \beta_0 + \beta_1 A_s + \beta_2 G_s + \beta_3 V_s + \sum_{k=1}^{2} \beta_{3+k} I[C_{k+1}]_s A_s + \beta_{5+k} I[C_{k+1}]_s G_s + \beta_{7+k} I[C_{k+1}]_s V_s + b_{0,s} + \epsilon_{i,s}.$$

In the above, $M_{i,s}$ is the morphometric feature's value for region i and subject s. The model includes an intercept (β_0 coefficient) and considers the individual impacts of age (A_s, β_1), gender (G_s, male=0, female=1, β_2) and total grey matter volume (V_s, β_3).

Regarding the impact of group (C_1 to C_3 for HC, ET_{pre} and ET_{post}, respectively), $I[C_k]_s$ is a dummy variable encoding whether subject s belongs to group C_k. Because of the presence of an intercept term in the model, only two dummy variables are needed to account for three groups. We model the interactions between group and the three confounds (*i.e.*, we enable distinct extents of confounding impacts across groups, as summarized by coefficients β_4 to β_9).

The term $b_{0,s}$ is the random effect for subject s (a subject-specific intercept), which follows a normal distribution with mean 0 and standard deviation σ_b. Finally, $\epsilon_{i,s}$ is the error term for region i and subject s, following a normal distribution with mean 0 and standard deviation σ.

The residuals of the model (including random effects, as well as group effects since they were not explicitly modelled) were used for all subsequent analyses.

Computation of morphometric similarity to HCs

For cortical brain regions, we considered three-dimensional (CT, SA, MC) data points for each subject. For non-cortical brain regions, we considered one-dimensional data points (regional volume), where univariate Gaussians are fitted and only two parameters characterize a distribution (the mean and standard deviation).

For each region, the HC data was modelled by a multivariate normal distribution with mean vector $\boldsymbol{\mu}$ and covariance matrix $\boldsymbol{\Sigma}$, which jointly describes the variance for each morphometric property (diagonal elements), and the covariance across them (off-diagonal elements; see [26] for further mathematical details). The best mean vector and covariance matrix estimators $\widehat{\boldsymbol{\mu}}$ and $\widehat{\boldsymbol{\Sigma}}$, in the log-likelihood sense, are trivially the data's arithmetic mean and covariance matrix.

The log-likelihood (LL) of a data point $\boldsymbol{x}$ (which represents the morphometric estimate[s] of a given subject before or after thalamotomy) to be issued from this distribution can then be computed as:

$$\mathcal{LL}_{\mathcal{N}}\left(\boldsymbol{x}|\widehat{\boldsymbol{\mu}},\widehat{\boldsymbol{\Sigma}}\right) = -\frac{1}{2}\ln\left(\sqrt{2\pi\left|\widehat{\boldsymbol{\Sigma}}\right|}\right) + (\boldsymbol{x}-\widehat{\boldsymbol{\mu}})^{\mathrm{T}}\widehat{\boldsymbol{\Sigma}}^{-1}(\boldsymbol{x}-\widehat{\boldsymbol{\mu}}).$$

References

1. Ségonne F, Dale AM, Busa E, Glessner M, Salat D, *et al*. A hybrid approach to the skull stripping problem in MRI. *Neuroimage*. 2004;22(3):1060-1075.

2. Fischl B, Dale AM. Measuring the thickness of the human cerebral cortex from magnetic resonance images. *Proceedings of the National Academy of Sciences U.S.A.*. 2000;97(20):11050-11055.

3. Desikan RS, Ségonne F, Fischl B, Quinn BT, Dickerson BC, *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.