## Image analysis

Image processing leveraged the open-source ANTsX software ecosystem (Tustison et al. 2021) with a particular focus on specific deep learning applications developed for neuroimaging made available for both Python and R users via the ANTsXNet (ANTsPyNet/ANTsRNet) libraries. Specifically, for the work described here, white matter hyperintensity segmentation and lobar parcellation based on the Desikan-Killiany-Tourville (DKT) cortical labels (Klein and Tourville 2012) employed the ANTsPyNet functions:

* sysu\_white\_matter\_hypterintensity\_segmentation and
* desikan\_killiany\_tourville\_labeling,

respectively. Note that in addition to the netework architectures being specified by the ANTsXNet functions, data (including both weights and ancillary image data, such as templates) are also available and automatically downloaded from <https://figshare.com> to a specified cache directory and stored for subsequent use.

**White matter hyperintensity segmentation.** In conjunction with the International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI) held in 2017, a challenge was held for the automatic segmentation of white matter hyperintensities using T1-weighted and FLAIR images (Kuijf et al. 2019). Image data from five separate collection sites were used for training and testing of algorithms from 20 different teams. The winning entry used a simplified preprocessing scheme (e.g., simple thresholding for brain extraction) and an ensemble () of randomly initialized 2-D U-nets (Falk et al. 2019) to produce the probabilistic output (Li et al. 2018). Importantly, they made both the architecture and weights available to the public. This permitted a direct porting to the ANTsXNet libraries with the only difference being the substitution of the threshold-based brain extraction with a deep-learning approach (Tustison et al. 2021).

**Lobar parcellation.** An automated, deep learning-based DKT labeling protocol for T1-weighted images was briefly described in (Tustison et al. 2021) where it was used to provide regional summary measures for the ANTsXNet cortical thickness pipeline. Data from multiple sites described in (Tustison et al. 2014) was used to train two networks—one for the “inner” (e.g., subcortical, cerebellar) labels and one for the “outer” cortical labels. Training was performed using ANTsRNet with trained weights being cross-compatible with ANTsPyNet as they are both Keras- based. Inputs include the T1-weighted image and spatial priors for each label being included as additional channels to enforce spatial constraints on the output. For both training and prediction, input T1-weighted images are skull-stripped (Tustison et al. 2021) and transformed to the space of a cropped version of the MNI152 template (Fonov et al. 2009) (also the space of the spatial priors described above). Both networks use the U-net architecture with attention gating (Schlemper et al. 2019). Inner and outer networks are characterized by 8 and 16 filters at the base layer doubling at each subsequent layer for four total layers.

After an individual T1-weighted is labeled with the cortical DKT regions, the six-tissue (i.e., CSF, gray matter, white matter, deep gray matter, cerebellum, and brain stem) segmentation network is applied to the skull stripped image. Cortical labels corresponding to the same hemispherical lobes are combined and then propagated through the non-CSF brain tissue, using a fast marching approach (Sethian 1996), to produce left/right parcellations of the frontal, temporal, parietal, and occipital lobes, as well as left/right divisions of the brain stem and cerebellum.

## References

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