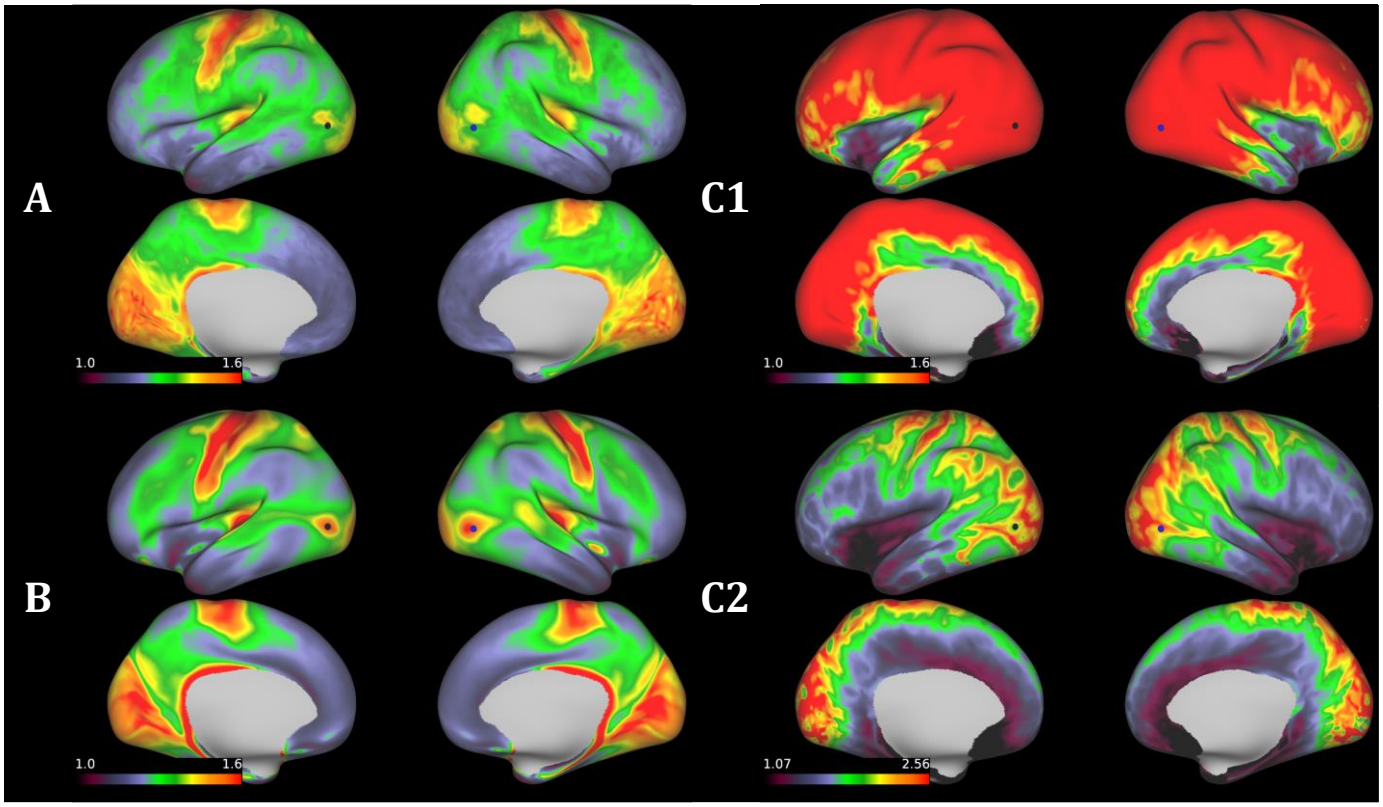
CBF processing pipeline

CBF measurements were available in 53 out of 54 non-diabetic controls and in 58 out of 61 T1D patients. The raw PCASL images were first motion-corrected using the MCFLIRT command of FSL (FMRIB Software Library, version 5.0.7) after selecting the first volume as template volume for the alignment. Mean control images of the ASL series were also computed to obtain images with enhanced contrast, to improve the coregistration between the perfusion maps and the anatomical scans. To reduce the effect of motion, the final averaged CBF maps were computed considering only the label-control pairs from the raw PCASL images that did not exceed the thresholds of 1mm for the head movement translations and 1 degree for the head movement rotations. The selection of these more stringent criteria than those used previously is particularly beneficial not only for the evaluation of small brain structures (e.g. basal ganglia), but also for neocortical areas. For example, with the used FOV equal to 210 mm, a rotation around the centre of the brain in one direction exceeding 1 degree would translate into peripheral voxel displacement of more than 1.8 mm. If combined with an eventual 1-mm shift, the total movement of peripheral voxels would exceed 2.8 mm, a threshold comparable to the size of imaging voxels. Motion correction of the pairs of label and control images with large motions will result in interpolation smearing and can introduce substantial subtraction errors into the mean CBF maps. In real life situations, the axis of the rotation would not be located in the centre of the brain, leading to much larger voxel displacement than described above.
To avoid bias in the final results introduced by the chosen motion correction criteria, we also considered maps obtained after removing the pairs exceeding the translation of 3mm (equal to voxel size). Not to penalize the signal to noise ratio (SNR) at the ROI level, maps produced with at least 30 control-tag pairs were considered for the statistical analyses.

CBF data from 3 non-diabetic controls and 6 T1D patients were excluded due to excessive motion as defined by the quality criteria (<30 pairs with motion less than 1mm of translation and 1° of rotation) or to other image quality issues, leaving 50 non-diabetic controls and 52 T1D patients (see Supplementary Figure 2).

Supplementary figure 1: Comparison of previous and current T2-weighed (T2w) protocols based on the resulting myelin (T1w/T2w ratio) maps. A – myelin map calculated with the current T2w sequence in a type 1 diabetes (T1D) patient. B – reference average myelin maps from the human connectome project for comparison. C – myelin map in an excluded T1D patient with the previous T2w sequence. C1 – with the same palette window [1.0 – 1.6] as in the images A and B. C2 – with a more adequate palette window [1.1 – 2.6] showing not only quantitative (relatively higher T1w/T2w ratios) but also qualitative changes (e.g. the absence of the area with higher T1w/T2w value close to the central sulcus and generally different pattern).



Supplementary Figure 2: Enrolment flowchart. ASL: arterial spin labelling; CBF: cerebral blood flow; T1w: T1-weighted; T2w: T2-weighted; T1D: type 1 diabetes mellitus