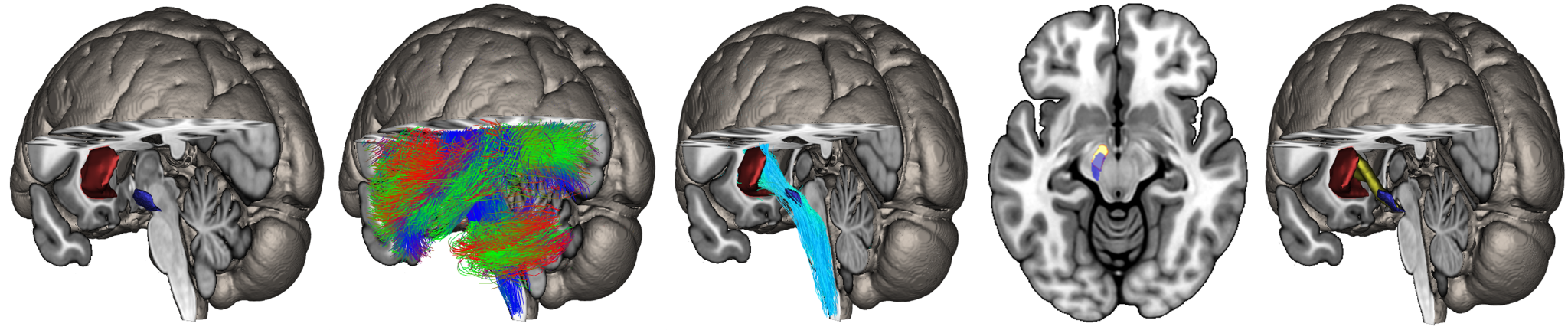
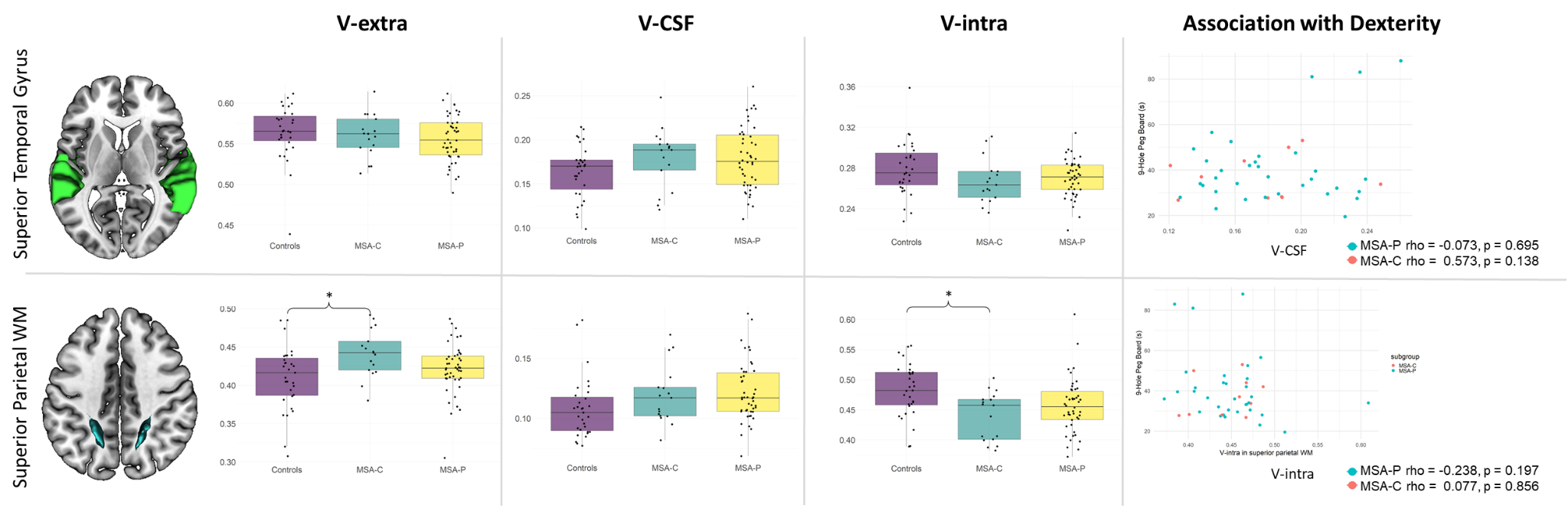
**Supplementary Methods**

A global tractography-based approach was used to identify the NST. For this, we relied on a normative connectome in the MNI space composed of 100 subjects from the Human Connectome Project database (mean age 29 ± 3.7; 64 females, 36 males; [www.humanconnectome.org](http://www.humanconnectome.org/)). Streamlines characterized by at least 1% overlap between the total streamline length and the ROI volume of the SN and the striatum (both obtained from the AAL3-atlas) were selected. From the parameter sets provided by the toolbox (10.1016/j.neuroimage.2010.09.016), we utilized the ‘superdense’ preset for our analyses. Fiber visit maps were rendered on a grid of resolution 2.5 × 2.5 × 2.5 mm3 by trilinear interpolation and smoothed by an isotropic Gaussian filter of 3 mm FWHM. The respective ROIs were warped from the MNI space to the individual patient space similar to the other ROIS.

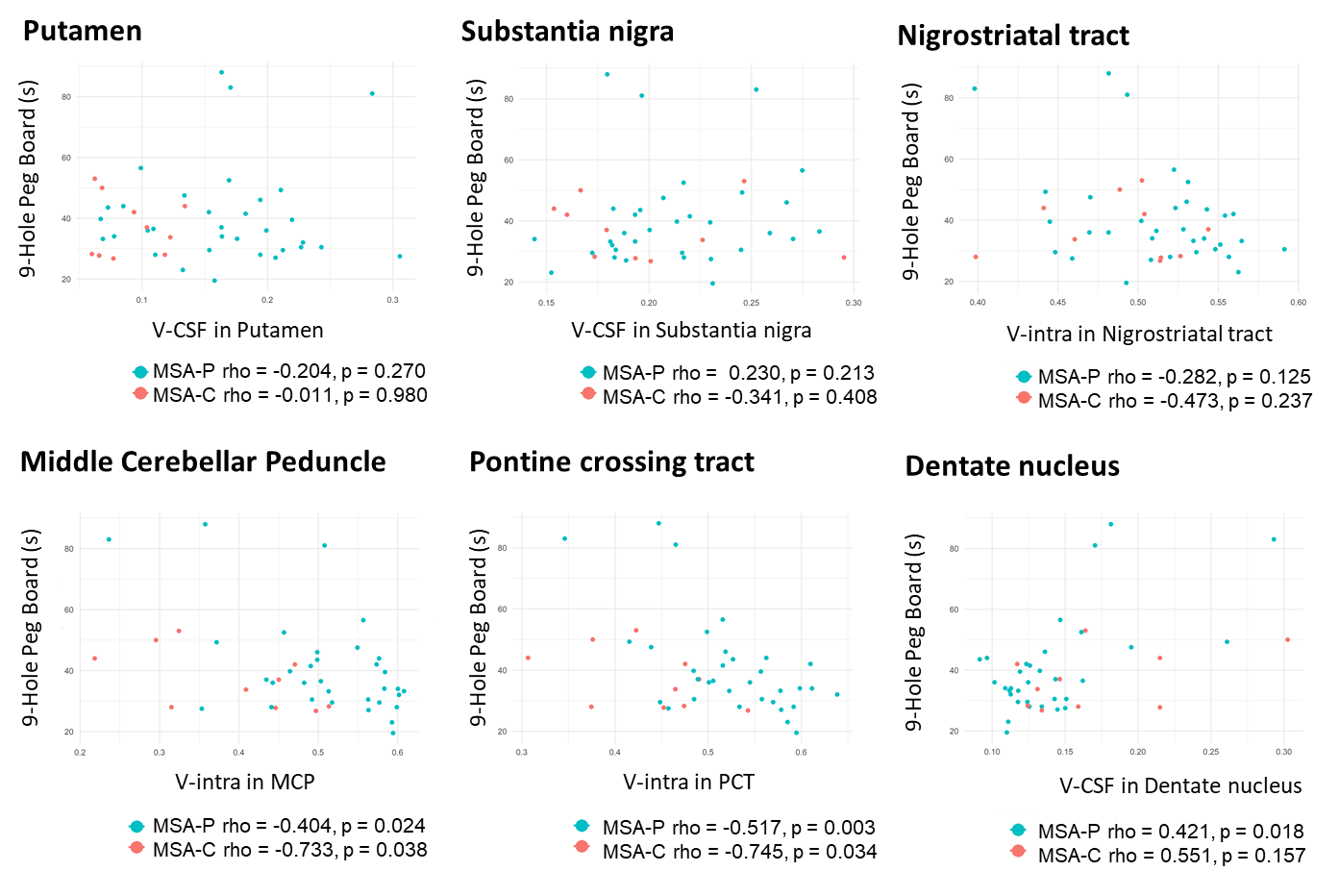
**Supplementary Figures**



**Supplementary Figure 1** Illustration of the identification of the nigrostriatal tract using a tractography-based approach. From left to right: In standard MNI space, the ROI of the substantia nigra (blue) and putamen (red) were defined using a probabilistic atlas. Subsequently, a normative connectome was used to identify the streamlines with at least a 1% overlap between the total streamline length and the ROI volumes. Fiber visit maps were rendered on a grid of resolution 2.5 × 2.5 × 2.5 mm3 by trilinear interpolation, smoothed by an isotropic Gaussian filter of 3 mm full-width at half maximum and transformed to a ROI (yellow).



**Supplementary Figure 2** Comparison of DMI metrics obtained from gray and white matter control regions potentially unaffected in MSA.



**Supplementary Figure 3** Association between V-CSF in the putamen, substantia nigra, and dentate nucleus or V-intra in middle cerebellar peduncle (MCP), pontine crossing tract (PCT) and nigrostriatal tract with 9-Hole Peg Board Performance. Each dot represents a single patient while blue depicts MSA-P and orange MSA-C.