Using surface connectivity atlases to measure striato-cortical "disconnection rate" in Huntington disease

L. Marrakchi-Kacem[1,2], C. Delmaire[3], A. Tucholka[4,5], P. Roca[1,2], P. Guevara[1,2], S. Lecomte[1,2], F. Poupon[1,2], J. Yelnik[6], A. Durr[6], J-F. Mangin[1,2], S. Lehericy[2,3], and C. Poupon[1,2]

[1]NeuroSpin, CEA, Gif-Sur-Yvette, France, [2]IFR49, Gif-Sur-Yvette, France, [3]CENIR, Pitié Salpêtrière Hospital, Paris, France, [4]Centre de Recherche Hôpital Ste-Justine, Montreal, Canada, [5]Université de Montréal, Montreal, Canada, [6]CRICM, Inserm/UPMC, Paris, France

Introduction

The striatum is directly connected to most cortical regions. Striatal projection zones of cortical afferents define territories, including sensorimotor, associative and limbic territories. Surface cortical connectivity atlases [1] allow the analysis of the connectivity existing between deep nuclei and the cortex and can be used to study cortico-striatal disconnection in diseases involving the basal ganglia, such as Huntington's disease. In this abstract, we used surface cortical atlases of the striatum nuclei to measure the rate of "disconnection" of the caudate nucleus and the putamen to predefined cortical regions of interest in a population of patients suffering from Huntington's disease. Atlases were built from a population of healthy subjects and from a population of Huntington's patients. We defined "the disconnection rate" as a measure of the percentage difference between the atlases of healthy subjects and Huntington's subjects taking healthy subjects as the reference. The obtained disconnection rates are potential biomarkers of Huntington's disease.

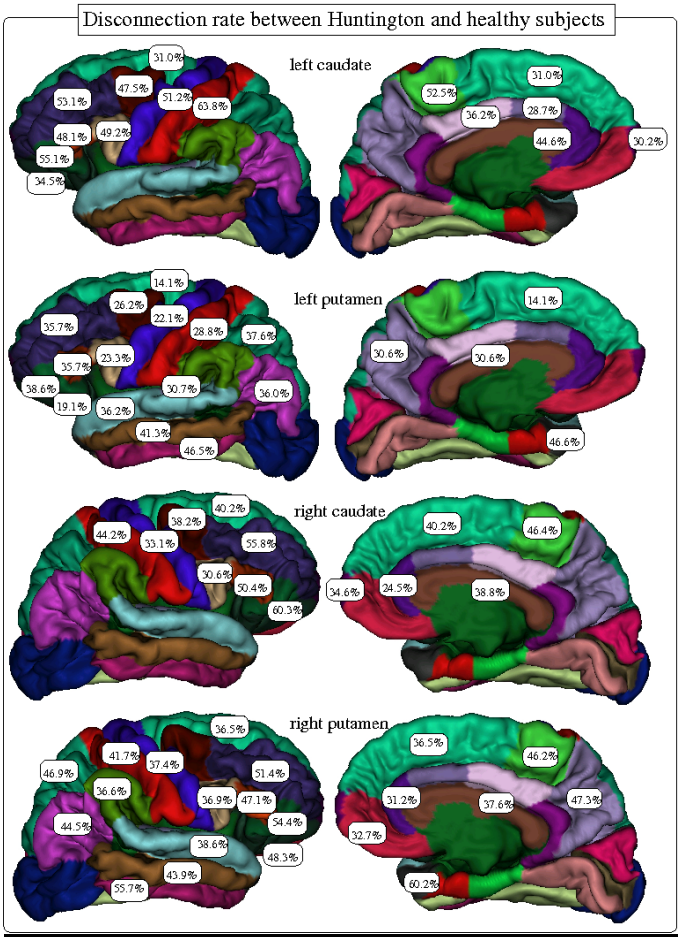
Material and methods

The surface connectivity atlases were built using a database containing DW- and T1-weighted MRI data from 17 healthy subjects and 19 Huntington's subjects that signed an informed consent. These subjects were part of the TRACK-HD study.

Acquisition **-** Data were acquired using a 3T Tim Trio MRI system (Siemens, Erlangen). Sequence parameters were as follows: **T1-weighted 3D MPRAGE** FOV=256mm, matrix 256x256, TE/TR=2.98ms/2.3s, TI=900ms, TH=1.1mm, Phase FOV=93.8%, 160 slices per slab, RBW=240Hz/pixel; **Single-shot twice refocused spin-echo DW-EPI** FOV=256mm, TH=2mm, matrix 128x128, TE/TR=86ms/12s, GRAPPA 2, partial Fourier 6/8, 80 slices, RBW=1630Hz/pixel, b-value b=1000s/mm², 50 directions; DW data were corrected from susceptibility artifacts using a double gradient echo phase difference map to get the associated field map and using a non linear resampling stemming from the field map.

Connectivity atlases **-** For each subject s, a local orientation distribution function (ODF) field was computed from the DW-weighted data using the analytical Q-ball HARDI model (SH order 6, λ_B=0.006,step=0.05mm) [2]. A streamline probabilistic tractography [3] was then applied to recover the whole brain connectivity using the following parameters (aperture angle 30°, 27 seeds per voxel) from a robust mask of the brain. The connectivity of each nucleus of the striatum was obtained by intersecting the resulting 3D ROIs corresponding to the deep nuclei stemming from an automatic segmentation tool (Nucleist [4]) based on T1-weighted data and the previous whole brain connectivity. The individual WM/GM interface was extracted from the T1-weighted data using Freesurfer [5]. An individual connectivity matrix was processed between the 4 nuclei of the striatum and the set of vertices of the WM/GM interface [6]. For each nucleus n and each vertex position *v* of the WM/cortex interface, the values $C_s(n,v)$ of the connectivity matrix represents the number of tracts linking each nucleus n to v. As a direct inter-subject vertex to vertex correspondence exists between all the WM/cortex interfaces (similar to [7]), an average $C_P(n,v)$ connectivity value can be computed for all the subjects of a given population for each nucleus and each vertex position. The set of values $C_P(n,v)$ for all the vertex positions v constitute the average surface connectivity atlas of the nucleus n for the population P. An average connectivity atlas was computed for each population and for each nucleus.

Cortical disconnection rate **-** For a given nucleus n, let $C_{HD}(n,v)$ and $C_H(n,v)$ be the average atlas of the Huntington population and the healthy population respectively. The rate of disconnection (DR) between n and a given cortical region r is defined as: $DR(n,r)= (C_H(n,r)- C_{HD}(n,r))/C_H(n,r)$. We computed the DR for each nucleus n of the striatum and some cortical regions of interest. The regions of interest were obtained using Freesurfer parcellation into gyri[8]. The most connected gyri were selected for each nucleus. A non parametric Mann Whitney test with a significance value α=0.05 was applied to the selected gyri to check whether they present a significant connectivity difference between the two populations [9]. The disconnection rate was computed for each nucleus on the gyri presenting a significant connectivity difference.



Results and discussion

The disconnection rates DR(n,ROI) obtained for each nucleus on the selected cortical regions are shown on the figure. This new measure identifies for each nucleus the cortical regions to which the connections were highly reduced. For the left caudate nucleus, the values ranged from 28.7% for the left caudal anterior cingulated gyrus to 63.8% for the left post central gyrus. For the right caudate nucleus, the DR values ranged from 24.5% for the right rostal anterior cingulate gyrus to 60.3% for the right pars orbitalis gyrus. The DR values for the left putamen vary from 14.1% for the left superior frontal gyrus to 46.6% for the left frontal pole gyrus. Finally the DR for the right putamen ranged from 31.2% for the right anterior cingulate gyrus to 60.2% for the right temporal pole gyrus.

Conclusion

We have defined a cortical "disconnection rate" computed from non normalized striato-cortical connectivity surface atlases. These average non normalized atlases were computed for each nucleus of the striatum. The disconnection rates allowed the quantification of the decrease in connections between the striatum and cortical regions of interest. These disconnection rates represent novel connectivity biomarkers of Huntington's disease.

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References

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