Distribution of the functional atrophy in the striatum territory of Huntington's patients

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Introduction

The striatum including the caudate and putamen nuclei is involved in numerous functional tasks. It ensures sensorimotor, associative and limbic functions. Each striatum nucleus can be subdivided into sensorimotor, associative and limbic territories that can overlap and that are connected to corresponding cortical regions of interest. Many studies have focused on the parcellation of the striatum into functional territories in humans[1,2,3] either using an histological marker [1] to build an atlas of the striatum nuclei subsequently registered to each new subject or using the cortico-striatal connectivity profile stemming from diffusion tractography[2,3]. In neurological diseases, it is of interest to measure the amount of atrophy of these functional territories. Nevertheless, if the ratio between the volume of each functional territory and the volume of the whole nucleus is computed using a parcellation of the nucleus into subterritories, the measure may not be accurate because these parcels don't take into account the existing overlap between functional territories. We propose a novel approach relying on the estimation of the ratio between the volume of each functional territory and the volume of the whole nucleus, using surface probabilistic maps of the striato-cortical connectivity. We used this ratio to evaluate the distribution of functional atrophy in the striatum territories for patients suffering from the Huntington's disease.

Material and methods

The probabilistic surface maps were built using a database containing diffusion-weighted (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 on a Tim Trio 3T 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, bandwidth=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, bandwidth=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.

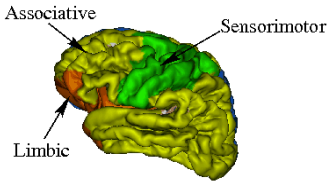
Surface probabilistic maps **-** For each subject s, a local orientation distribution function (ODF) field was computed from the DW-weighted data using the analytical Q-ball HARDI model (SH order 6, λ_B=0.006,step=0.5mm) [4]. A streamline probabilistic tractography was then applied to recover the whole brain connectivity with 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 [5]) 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 [6]. An individual connectivity matrix was processed between the 4 nuclei of the striatum and the set of vertices of the WM/GM interface [7]. 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. The probability of connection between n and v is the ratio between $C_s(n,v)$ and the global number of fibers connecting n to the cortical mantel of the subject s: $p_s(n,v)= C_s(n,v)/(\sum_{v'} C_s(n,v'))$.The set of values $p_s(n,v)$ for all the vertex positions v constitute the surface probabilistic map of connectivity of the nucleus n for the given subject s. For a given cortical region of interest, the probability of connection $p_s(n,r)$ between a nucleus n and a given cortical region of interest r can be computed by integrating the values of $p_s(n,v)$ over the region r.

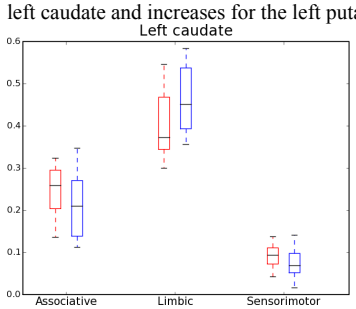
Cortical ROIs **–** An expert delineated manually 3 functional territories (associative, limbic and sensorimotor) on the cortical surface for each hemisphere for 10 healthy subjects. For each segmented subject, a texture was computed from the manual delineation of cortical territories and the WM/cortex interface computed from Freesurfer. An average texture was then computed using the inter-subject direct correspondence of the obtained textures (similar to [8]).

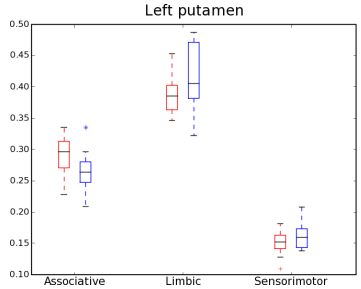
Distribution of atrophy **–** If we assume that the number of fibers crossing a region of a functional territory of a nucleus is proportional to its volume, the probability of connection between n and r is equal to the ratio between the volume of the region of the nucleus from which the connections come and the volume of the nucleus. By computing this ratio for each nucleus and for each functional cortical region, we can evaluate the distribution of the atrophy of each functional territory of the nucleus and compare it between the population of healthy subjects and the population of Huntington's subjects. The obtained values were compared between the two populations using a Mann-Whitney test.

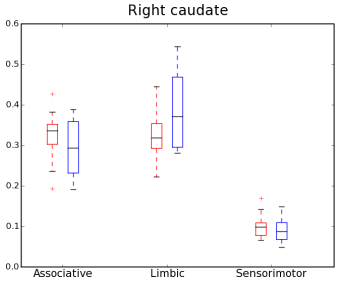
Results and discussion

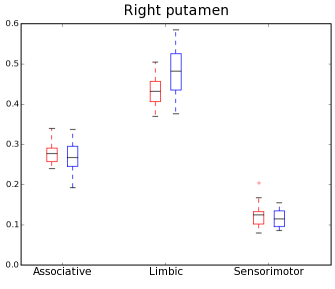
The Mann-Whitney test showed that for the left caudate and putamen, the proportions of the associative and limbic territories are significantly different between the two populations. For the right caudate and putamen, only the proportion of limbic territories are significantly different. The median values of the ratio and their quartiles obtained for each functional territory are represented in the figures below for each nucleus and for healthy subjects (in red) and patients with Huntington's disease (blue). For the caudate nuclei the median value for the proportion of associative territory is lower for patients and the median value for the proportion of the limbic territory is higher with a large variability across subjects. For the putamen, the median value for the proportion of the associative territory decrease in patients and the median value for the proportion of the limbic territory increase. Concerning the sensorimotor territory, the median value for its proportion is stable in the right hemisphere. It decreases for the left caudate and increases for the left putamen.











Conclusion

We have proposed a novel method to measure the proportion of each functional territory in the striatum. We have used this measure to study the distribution of each functional territory inside the striatum and to detect the variation of this distribution linked to Huntington's disease. We have observed a difference in distribution of the functional territories in Huntington patients, i.e. a decrease in the proportion of the associative territory and an increase in the proportion of limbic territory. This measure may constitute a novel biomarker of Huntington's disease.

This work was founded by the Ecole des Neurosciences Paris-Ile-de-France, the ANR MNP, and the CHDI High Q Foundation

References

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