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DOTTORATO DI RICERCA IN
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STUDIO ANATOMO-FUNZIONALE INTEGRATO
DELLA SOSTANZA BIANCA CEREBRALE
E COMPUTAZIONE DI UN ATLANTE FUNZIONALE SOTTOCORTICALE

Settore Scientifico Disciplinare MED/26

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ABSTRACT

INTRODUCTION AND AIMS

Over the last 20 years the study of brain functions experienced a huge impulse due to the technical improvements in the imaging and neurosurgical cortico-subcortical direct electrical stimulation (DES) procedures. Particularly, functional MRI (fMRI), DES and diffusion tensor imaging (DTI) allowed the *in vivo* study of functional organization and white matter (WM) connections. The integration of data provided by these different techniques opened a new door in the study of the brain, leading neuroscientists and neurosurgeons in the connectomic era. This conceptual evolution renewed the interest also for the structural study of brain connections with blunt dissection, in order to improve and confirm data provided by DTI.

Considering that DES is, since now, the only direct and specific method to explore the functional role of subcortical bundles, we aimed to a study integrating blunt dissection, according to the technique described by Klingler, DTI and DES during neurosurgical procedure for resection of low-grade gliomas (LGGs).

Aims of the study are:

- 1) definition of course and terminations of the main WM fascicles;
- 2) production of antomo-topographical data, including course and reciprocal relationships of different association, projection and connection bundles, in order to produce anatomo-functional details for the improvement of surgical approach to intra-axial lesions.
- 3) computation of the first functional atlas of the human WM and of a probabilistic map of WM resectability, using data provided by DES during awake surgery with intra-operative neuropsychological monitoring.

MATERIAL AND METHODS

Dissection with Klingler's technique

The sample hemispheres were injected with a formalin solution at 10% (through carotid and vertebral arteries) and then fixed for 40 days, with following freezing (-20°) for 20 days. We performed a blunt dissection (with wooden spatula) according to the cortex sparing technique.

Tractography

60 direction diffusion weighted imaging (DWI) was acquired (single-shot multislice spin echo planar with following parameters: 40 slices; slice thickness: 2.4 mm; matrix 256 x 256; TR: 10 000; TE: 92.7; flip angle: 90) for the tractography. Post-processing and tractography calculation were obtained with: FMRIB Software Library, <http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/>; Diffusion Toolkit 0.6.1 e TrackVis 0.5.1, <http://trackvis.org>.

Direct cortico-subcortical electrical stimulation

All the patients underwent to awake surgery with clinical and neuropsychological intra-operative monitoring. For the functional and resection Atlas computation, 339 functional responses in 130 patients were collected. Different other cases were added in the anatomical papers. All the patients underwent to pre- and post-operative (3-months) MR for the evaluation of resections and the collection of the regions of interest (ROIs) of functional responses, surgical cavities and residual tumors.

White matter Atlas computation and resection map

All the ROIs and the MR were co-registered to the common MNI 152 space, such as the subcortical DTI probabilistic Atlas by Thiebaut de Schotten (2011) and cortical AAL Atlas (Tzourio-Mazoyer et al, 2002). It allowed the computation of the probabilistic cortico-subcortical resection map and of the functional atlas of human WM (for language, sensory and motor, visual and visuo-spatial tasks).

RESULTS AND DISCUSSION

The first anatomo-structural study of the inferior fronto-occipital fascicle (IFOF) with blunt dissection and DTI and a second study integrating DES data of 6 patients, showed the full course of IFOF and demonstrated a new deep component terminating in the dorso-lateral pre-frontal (DLPFC). The results confirmed the involvement of this bundle in the semantic network and,

considering the longest course of this bundle with terminations in all the encephalic lobes, we hypothesized also a possible multi-functional role for IFOF.

The study of the optic radiation (OR) with Klingler's dissection, DES data of 3 patients and DTI reconstructions integrated, allowed us to show more details in the course and anatomo-functional relationships with other bundles. We divided the OR in two components. The superior OR was demonstrated to cover the lateral wall, the roof of the trigone and the roof of the temporal horn of lateral ventricle and it is completely overlapped from the IFOF fibers all over its course, up to external capsule (EC). The inferior OR covers the inferior third of the lateral wall of the trigone and the lateral wall and floor of the temporal horn up to the tip, where it arches around to form the Meyer's Loop.

The anatomo-functional (blunt dissection, DES and DTI reconstructions) of the temporo-parieto-occipital carrefour demonstrated the reciprocal relationships and the functional roles of different bundles: arcuate fascicle (AF), indirect and direct components of the superior longitudinal fascicle (SLF), IFOF, pyramidal tract (PT) and posterior thalamic radiation (PTR). Moreover, we identified two possible functional tailored approaches for dorsal and ventral lesions harboring this region.

Finally, the unique and large series including 339 functional responses in 130 patients allowed the computation of a volumetric map of cortico-subcortical resection. Considering the potential large resections in areas commonly considered high eloquent, it confirmed the plastic potential of the human brain. Moreover, the integration of DES data generated a detailed atlas of functions distribution. Finally, the matching of DES data with the DTI probabilistic atlas confirmed the functional role of different bundles (IFOF for semantic network, AF for phonological, indirect and direct component of the SLF for verbal apraxia and semantic retrieval), led to functional hypotheses regarding other bundles (i.e. subcallosal fascicle or Aslanct tract for motor planning) and demonstrated the crucial role in functional execution of projection bundles (i.e. PT, PTR and OR).

CONCLUSIONS

The integration of data provided by neuroradiological imaging, neurosurgery, neurophysiology and anatomical studies is crucial for solution of anatomical and functional questions still opened.

The anatomo-functional study of cerebral connectivity is crucial for the refinement of neurosurgical techniques, which became now a unique and reliable opportunity for neuroscientific purposes.

The chance to compute this first and updatable Functional Atlas of Human WM with DES data is not to be considered the arrival but, definitely, it is the essential background for the comprehension of the complex "wires and networks" system, subserving the brain functions.