Neural correlates of spatial awareness revealed by MR DTI tractography and intraoperative subcortical mapping

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Introduction
Brain mechanisms underlying spatial awareness have recently become intensely disputed: particularly, subcortical networks including prefrontal and parietal areas seems to be important for spatial attention and space-related behaviour [1–2]. Dysfunction of these networks results in unilateral spatial neglect, a complex and disabling syndrome that is typically associated with right hemisphere lesions [3]. Neglect is characterized by an impairment of awareness of contralesional left half of space, objects and mental images. Recently, damage to the superior longitudinal fascicle (SLF), a major association fiber pathway connecting parietal and frontal cortical regions, has been described in neglect patients [3]. Further evidence has come from intraoperative subcortical stimulation during brain surgery, by temporarily inactivating restricted cerebral regions to map cognitive functions in humans [4].

Aims of this study are: 1) to perform DTI preoperative tractography in patients with right cerebral gliomas by segmenting the four subdivisions of SLF; 2) to combine tractography results with identification of functional subcortical sites during intraoperative line bisection test in order to assess the contribute of this fascicle in spatial attention networks.

Materials and Methods
MR DTI data were acquired from six patients with cerebral gliomas (4 oligodendrogliomas, 2 GBM). Imaging was performed on a 3T MR scanner (Philips Intera, Best, The Netherlands) with a 8-channel head coil. DTI data were collected using a single-shot echo planar imaging (EPI) sequence (TR/TE 8986/80 ms) with parallel imaging (SENSE factor, R = 2.5). 32 diffusion gradient directions (b=1000 s/mm²) and one image set without diffusion-weighting were obtained. A field of view of 240 × 240 mm² and a data matrix of 96 × 96 were used and this led to isotropic voxel dimensions (2.5 × 2.5 × 2.5 mm³). Acquisition coverage extended from medulla oblongata to the brain vertex (56 slices, no gap). The sequence was repeated two consecutive times and data were averaged off-line to increase signal-to-noise ratio; DTI datasets were aligned off-line to the echo-planar volume without diffusion weighting on a PC workstation using the AIR (Automatic Image Registration) software to correct artifacts due to rigid body movement during scan acquisition. 3D Fast Field Echo (FFE) T1-weighted imaging (TR/TE 8/4 ms; image resolution equal to DTI) was performed for anatomic guidance.

Preoperative tractography was performed using Dti Studio version 2.4.01 software (Jiang H, Mori S, Radiology Department, Johns Hopkins University, Baltimore, MD, USA) to reconstruct superior longitudinal fascicle and to segment its four subcomponents with a two-ROIs approach, according to the subdivision described by Makris and colleagues [5]. Inferior fronto-occipital fascicle (IFO) was also reconstructed in all patients. Data were transferred to the neuronavigation system as described in [6]. Surgery was performed in asleep-awake anesthesia, allowing to correlate functional subcortical sites identified by intraoperative subcortical mapping with fiber tracts depicted by tractography.

Results
Preoperative segmentation of the four subcomponents of SLF by DTI tractography was obtained in all patients. During subcortical mapping, a rightward deviation on line bisection test indicated the stimulation of an area involved in spatial awareness, whose electrical inactivation evoked neglect. In five patients subcortical mapping demonstrated a significant correspondence between the stimulated sites corresponding to fiber tracts and the second subdivision of SLF (blue, fig.1), that extends from the angular gyrus to the caudal-lateral prefrontal regions. No significant rightward deviation was observed by stimulating the first or third subdivision of SLF (green and yellow respectively, fig.1) or inferior fronto-occipital fascicle (light blue, fig.1).

Conclusions
Combination of preoperative tractography and intraoperative mapping confirms the hypothesis that the long-range white matter pathways connecting parietal and frontal areas are involved in mechanisms of spatial awareness; particularly, disruption of the second branch of SLF seems to be critically associated with unilateral spatial neglect.