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Topography of acute stroke in a sample of 439 right brain damaged patients

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ABSTRACT

Knowledge of the typical lesion topography and volumetry is important for clinical stroke diagnosis as well as for anatomo-behavioral lesion mapping analyses. Here we used modern lesion analysis techniques to examine the naturally occurring lesion patterns caused by ischemic and by hemorrhagic infarcts in a large, representative acute stroke patient sample. Acute MR and CT imaging of 439 consecutively admitted right-hemispheric stroke patients from a well-defined catchment area suffering from ischemia ($n = 367$) or hemorrhage ($n = 72$) were normalized and mapped in reference to stereotaxic anatomical atlases. For ischemic infarcts, highest frequencies of stroke were observed in the insula, putamen, operculum and superior temporal cortex, as well as the inferior and superior occipito-frontal fascicles, superior longitudinal fascicle, uncinate fascicle, and the acoustic radiation. The maximum overlay of hemorrhages was located more posteriorly and more medially, involving posterior areas of the insula, Heschl's gyrus, and putamen. Lesion size was largest in frontal and anterior areas and lowest in subcortical and posterior areas. The large and unbiased sample of stroke patients used in the present study accumulated the different sub-patterns to identify the global topographic and volumetric pattern of right hemisphere stroke in humans.

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1. Introduction

The area of damaged tissue in stroke follows patterns determined by the structure of the vascular trees (Stoeckel et al., 2007; Lee et al., 2009). Knowledge of typical lesion patterns is crucial in clinical stroke diagnosis as well as in anatomo-behavioral studies using statistical techniques such as voxel-based lesion-behavior mapping (Bates et al., 2003; Rorden et al., 2007). Nonetheless, studies describing the anatomy of brain damage are rare and often focused on subpopulations of strokes as for example patients with aphasia (Mirman et al., 2015; Caviness et al., 2002), included small sample sizes, and/or were based on acute perfusion MRI (Stoeckel et al., 2007; Caviness et al., 2002; Phan et al., 2005, 2007), which is not necessarily equivalent to final lesion demarcation (Neumann-Haefelin et al., 1999). A study by Lee et al. investigated a large sample of 205 patients. (Lee et al., 2009) Their results lacked a detailed topography as they concentrated on a binary classification (lesioned vs. non-lesioned) of large regions of interest (ROIs). Moreover, the study was restricted to infarcts of the PCA territory. To our knowledge the largest sample of lesion data has recently been published by Mah et al. (2014). The authors evaluated 581 left or right hemispheric stroke patients who had obtained diffusion weighted MR imaging, covering all vascular trees. Unfortunately, no descriptive information (location, size, phase of stroke, etc.) from the lesion groups and the illustrated anatomical overlay was provided.

The present study aimed to analyze a large, representative sample of stroke patients and describes lesion size and topography caused by ischemic and by hemorrhagic infarcts. To avoid any loss of representativeness individuals should be included independent of the imaging modality applied at admission. The latter is of relevance since in many stroke centers, a dominant brain imaging method applied at admission is CT with advantages typically including speed, cost, and reduced exclusion criteria relative to MRI. In clinical routine, there is a tendency to examine patients with severe and clear stroke symptoms at admission by CT imaging, since the dominant interest in those cases is to quickly identify hemorrhages. Contingent upon individual on-site organization achievement of this purpose is often faster and definitely cheaper by CT than by MR imaging. To exclude a systematic bias of our sample towards patients with less severe and less clear symptoms

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on admission, the present analysis should be based not only on acute MR but also on acute CT imaging.

2. Methods

2.1. Patient selection

Neurological patients admitted between 1999 and 2013 to the Centre of Neurology at Tübingen University Hospital were screened for an acute first unilateral, right-hemispheric stroke as indicated either by magnetic resonance (MR) imaging or computed tomography (CT). Patients with left-hemisphere stroke, with diffuse, bilateral, or cerebellar brain lesions, with previous large-artery or embolic stroke or pathological morphological changes of brain anatomy (e.g. massive brain atrophy), patients with tumors, patients with marked anatomical distortion due to intracerebral bleeding, patients who did not survive the acute stage of stroke, and patients without obvious lesion shown in MRI or CT were excluded. We included 439 patients (188 f, 251 m) with an average age of 62.4 years (SD = 13.4) at stroke onset. Of these patients, 367 had an infarct and 72 a hemorrhage. All patients or their relatives gave informed consent to participate in our study, which was performed according to the ethical standards laid down in the 1964 Declaration of Helsinki.

2.2. Imaging and lesion mapping

For all patients, an acute lesion was demonstrated by either CT or MR imaging. If both scan modalities were available, MR scans were preferred. As the validity to accurately identify stroke differs between imaging modalities dependent on time since stroke, under both protocols the initial scanning optionally was repeated during the following days until a firm diagnosis could be made and the infarcted area became clearly demarcated such that a clinically experienced researcher or a clinician experienced in lesion mapping could clearly identify lesion borders. The final scans were used for the present study. The present study included lesions that were demonstrated by using MR imaging in 210 cases and by CT in 229 cases. Time between stroke onset and imaging was 4.2 days (SD = 7.0) on average. In the subjects who underwent MRI scanning, we used diffusion-weighted imaging (DWI) in the hyper-acute phase until 48 h after stroke onset and T_2-weighted fluid attenuated inversion recovery (FLAIR) imaging in later stages after stroke onset.

For a majority of patients ($n = 274$) CT or MR imaging data were available in digital format. For these patients, the lesion was manually delineated on axial slices of the individual CT or MR scans using MRIcron (www.mccauslandcenter.sc.edu/mricro/mricron). Normalization of CT or MR scans was performed by using the Clinical Toolbox (Rorden et al., 2012) under SPM8 (www.fil.ion.ucl.ac.uk/spm), which provides age-specific templates oriented in MNI space for both CT and MR scans. If available, the MR scans were co-registered with a high-resolution T_1-weighted structural scan in the normalization process. For the remaining patients ($n = 165$) admitted before digital scans became available, lesions were drawn manually on slices of the T_1-weighted 'ch2' template MRI from the Montreal Neurological Institute (www.bic.mni.mcgill.ca/cgi/icbm_view) which is distributed with MRIcron. For the slices with the z-coordinates −40, −32, −24,

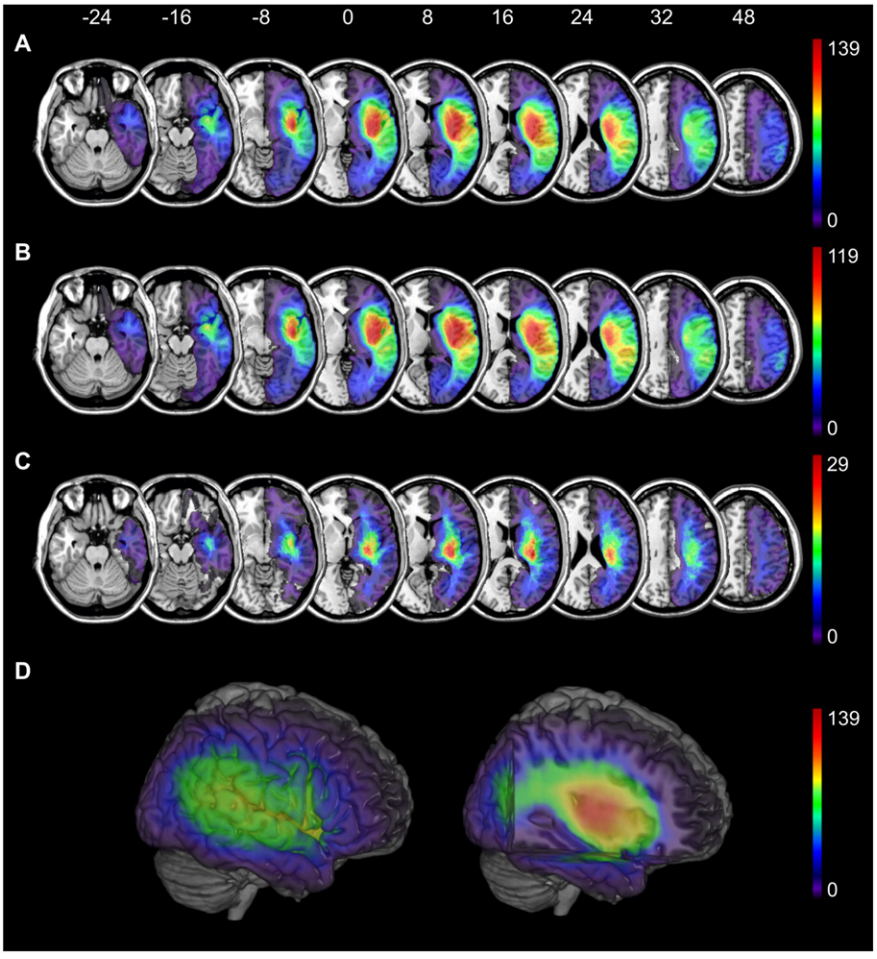

Fig. 1. Simple overlay plots for (A) all 439 acute right brain damaged patients, (B) for infarcts only ($n = 367$), (C) for hemorrhages only ($n = 72$), and (D) a 3D-rendered overlay plot for all 439 acute right brain damaged patients.

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