Lesion topography of posterior cerebral artery infarcts

T. Benke a, *, F. Dazinger b, R. Pechlaner a, K. Willeit a, J. Clausen c, M. Knoflach a

a Clinic of Neurology, Medical University Innsbruck, Austria
b Clinic of Neuroradiology, Medical University Innsbruck, Austria
c Centre of Neurology, Herie-Institute for Clinical Brain Research, University of Tübingen, Germany

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ABSTRACT

This study analyzed the topography of acute ischemic stroke in the posterior cerebral artery (PCA) territory. We studied 84 patients with unilateral ischemic PCA stroke. Patients were classified according to lesion levels as cortico-subcortical (superficial), combined (cortical and mesodiencephalic) or isolated thalamic. To receive a lesion map, data from acute MR and CT imaging were normalized and labelled automatically by mapping to stereotaxic anatomical atlases. Cortical lesions accounted for 41.7%, combined for 36.9%, and isolated thalamic lesions for 21.4%. The maximum overlay of ischemia and, thus, highest occurrence of PCA ischemic stroke was found in the ventral and medial occipito-temporal cortex and adjacent white matter association tracts. Dorsal and peripheral segments of the occipito-temporo-parietal region were only rarely lesioned. This configuration was similar in both hemispheres. Consistent with this lesion pattern, visual field defects (VFD) were the most frequent signs, followed by sensorimotor signs, dizziness and sopor, cognitive and oculomotor deficits, and ataxia. The three vascular subgroups differed not only by their anatomical lesion profile and lesion load, but also by their clinical manifestation; although patients with combined and thalamic lesions were significantly younger, they were more disabled than participants with cortical lesions. VFD were only found in cortical and combined, and oculomotor deficits only in mesodiencephalic lesions. White matter lesions were common in the cortico-subcortical and the combined group. Basal occipito-temporal and calcarine regions, and neighbouring white matter tracts have the highest risk of ischemia in acute PCA stroke.

1. Introduction

Stroke management depends on accurate knowledge of the arterial territories. Especially in acute stroke care a quick and reliable attribution of neurological deficits to a vascular territory and estimation of infarct size based on clinical findings might aid in treatment decisions like thrombolysis, thrombectomy or aggressive loading of antplatelet therapies. Compared with medial cerebral artery (MCA) ischemia, relatively little research has been performed regarding infarcts of the posterior cerebral artery (PCA) and their territorial distribution. The PCA supplies brainstem and thalamic territory (proximal, deep or penetrating branches; P1, P2), as well as temporal, calcarine, and parieto-occipital arteries (superficial branches; P3, P4) ([27,36], [35]). PCA strokes account for 10%–26% of all ischemic stroke ([15,48]). Frequent clinical characteristics of PCA infarction include visual-field defects (VFD), sensorimotor symptoms [3] and disturbances of cognition ([6,11,15,24]). A subset of patients with PCA infarcts exhibits typical MCA signs such as aphasia, spatial neglect or hemiparesis, but at the same time does not have the classic findings of a PCA stroke [32]. PCA infarcts have a wide range of infarct locations, also including atypical infarct distributions ([18,27]). This diversity is related to variations of vessels and supply territories in the posterior circulation, as well as inter-subject variability ([12,19,34,39,46]. Most previous reports evaluated either superficial [6] or deep PCA infarction [38], while studies covering both types have been rare. Some studies have included concomitant infarcts in other territories ([24,25,27,42] or have targeted only single structures like the hippocampus ([26,43]. A probabilistic map derived from a relatively small sample showed that most acute PCA infarcts were located in the medial and basal region, yet without detailed information regarding distinct anatomical structures or clinical correlates [35]. Since PCA stroke has several lesion patterns which differ as to their prevalence and stroke mechanism ([6,15,27,36], it seems interesting to compare lesion levels (i.e., cortical, thalamic and combined lesions) of PCA infarcts. This separation is also important since combined lesions result from vascular pathology involving both, deep-penetrating (P1, P2) as and well as superficial (P3, P4), whereas

* Corresponding author at: Department of Neurology, Medical University Innsbruck, Anichstr. 35, A-6020 Innsbruck, Austria.
E-mail address: thomas.benke@i-med.ac.at (T. Benke).

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cortical (superficial) lesions from occlusion of distal (P3 and P4) branches of the PCA, and the thalami receive their blood supply from both posterior and anterior circulations, with several known variations ([2,38]). Furthermore, occipital and temporal white matter connections like the optic radiation, cingulum, splenium or the inferior longitudinal and occipito-frontal fasciculus have been intensively investigated ([4,9,17,44]). However, it is still unclear which components of these tracts and fibres are damaged in PCA stroke. A further issue is that previous studies of PCA stroke topology have used visual analysis to assess lesion sites and size, without registration to a standard brain template ([8,18]). Therefore, we evaluated both, deep and superficial PCA infarcts using normalized MR images which were then processed for lesion plots and automatic anatomical labelling. A sample of isolated thalamic lesions was also included. We were interested to study the topographical diversity of acute PCA stroke, to identify regions with the greatest risk of infarction and to investigate the clinical profile of the three lesion levels.

2. Methods

2.1. Patients

The study was approved by the Ethic Committee of the Medical University of Innsbruck, Austria (protocol number 2010-UN4204). Patients gave informed, written consent to participate. PCA strokes were prospectively included from the stroke unit of the Department of Neurology, Medical University of Innsbruck, Austria between 5/2010 and 5/2018. Inclusion criteria comprised acute, first-ever, symptomatic, unilateral ischemic infarcts involving one or more superficial or deep PCA territories. Patients with concomitant lesions in the vertebrobasilar or cerebellar territory were excluded. We also excluded patients aged >90 years, severe brain atrophy, previous brain injury, or extensive white matter lesions (Fazekas score > 2). Infarcts were diagnosed via MRT or CT by an expert neuroradiologist (FD). Participants were allocated to three groups according to their lesion topography ([27,36]). In the cortical (superficial) PCA infarct group patients suffered from lesions of the occipital and/or posterior temporal cortex and the adjacent white matter; the thalamic group included uni- and bilateral isolated thalamic infarcts, whereas patients in the combined group had both, cortical, white matter and thalamic lesions.

2.2. Clinical assessment

Owing to the situation of stroke emergency, only a routine neurological examination was performed at admission evaluating consciousness, sensorimotor and oculomotor function, visuosperception, basic language functions and orientation. We recorded signs at admission, the initial NIH Stroke scale (NIHSS) and the modified Rankin score (mRS). Stroke etiology was classified according to TOAST criteria [1]. Macroangiopathy was defined as clinical and brain imaging findings of either significant (>50%) stenosis or occlusion of a major brain artery, presumably due to atherosclerosis. Microangiopathy was diagnosed in patients with (1) a subcortical lacunar infarct smaller than or equal to 1.5 cm on CT or 2.0 cm on MRI, (2) absence of cardiac sources for embolism, and (3) lack of stenosis >50% in the ipsilateral extracranial arteries. Cardioembolism was suspected when a cardiac source for a diagnosis of cardioembolic stroke was identified. Other determined etiology included rare cases of stroke such as, e.g., polycythemia or arterial dissection; etiology was labelled unknown when causes of a stroke could not be determined with any degree of confidence [21]. Hypertension, type 2 diabetes (HbA1c 6.0-6.4%) and diabetes (HbA1c > 6.5%), smoking, hyperlipemia, and atrial fibrillation (persistent or paroxysmal) were assessed as main vascular risk factors. Visual fields were assessed by standard neurological confrontation technique and by static perimeter testing (Eye-Suite, Haag-Streit Diagnostics); a computer-based test of visual target detection (flicker stimuli) in both hemifields (TAP, (Zimmermann, Fimm 2009)) was also used. The pattern of stimulus omission allows for a classification of VFD in normal perception, homonymous hemianopia and superior or inferior quadrantanopia with good sensitivity as compared with the standard Goldmann perimetry (Hildebrandt, Spang, Ebke 2002). In patients who had problems with fixation on the TAP (n = 8), visual fields were assessed only by confrontation method.

2.3. Lesion analysis

MRI and CT imaging was performed as part of the routine stroke work-up. Acute ischemic stroke lesions were identified by CT in 10, and by MRI in 74 patients as part of the routine radiological investigation. CT Images were obtained on a Siemens Somatom FLASH CT scanner with 120 kV and 290 m As. MRI scans were obtained on either a 1,5 T Magnetom Aera or 1,5 T Symphony TIM scanner (both Siemens, Erlangen, Germany). The standard stroke protocol included DWI and T2 sequences. For DWI we used a standard sequence in transversal orientation (45 slices, matrix = 128 × 128 pixel, voxel size = 1.8 × 1.8 × 3 mm, repetition time = 7.3 s, echo time = 97 ms with a b-factor of 1000 s/mm2). T2 (repetition time = 7730 ms, echo time = 90 ms, voxel size = 0.7 × 0.7 × 2 mm) was performed as transversal orientation FLAIR (repetition time = 8500 ms, echo time = 95 ms, voxel size = 0.9 × 0.9 × 3 mm), in coronor orientation TOF-MRA (repetition time = 27 ms, echo time = 7 ms, voxel size = 0.4 × 0.4 × 0.6 mm), and with 3D reconstruction SWI (repetition time = 50 ms, echo time = 40 ms, voxel size = 0.9 × 0.9 × 2.2 mm) in transversal orientation. Brain scans that showed the greatest extent of damage on transverse slices of diffusion weighted (DWI), or T2 FLAIR-weighted MR, or on CT images were used for lesion analysis. Lesions were delineated by trained raters (TB, JC) either manually using the MRicron software (http://www.www.mricron.com/mricron) or semi-automatically with the Clusterize algorithm ([13,16]). This algorithm was integrated into a SPM toolbox (http://www.medizin.uni-tuebingen.de/kinder/en/research/neuroimaging/software/) and used with SPM8 and running under Matlab R2016b (http://www.mathworks.de). The reconstructed 3D lesion map was visually checked for imperfections and discrepancies from the original MRI or CT slices, and manually adjusted, if necessary using the MRicron software. The 3D brain scan was spatially normalized to a standard brain template using a combination of MRicron and SPM (http://www.fil.ion.ucl.ac.uk/spm) as implemented in the Clinical Toolbox (https://www.nitrc.org/projects/clinicaltb/). Separate CT and MRI normalization templates were used for both imaging modalities [37]. The normalized lesion images were used as a region of interest (ROIs) for subsequent analysis in MRicron to compute group comparisons and overlay plots. The built-in interpolation algorithm of MRicron was used to compute an estimate for lesion volumes.

2.4. Anatomical lesion labelling

Each normalized lesion map was overlaid on top of the MNI background-3d slice image of MRicronGL (https://www.meccauslandcenter.ac.uk/mricrongl). Automatic anatomical labelling was performed with the AAL atlas [45] for grey matter regions and the NATBRAIN atlas [10], (https://www.natbrainlab.co.uk) for white matter tracts. A profile was created for each patient depicting which of the following regions in the PCA supply area were included in the ischemic lesion: occipital gyri (GO), superior, middle, inferior), optic radiation (OR, superior, inferior, combined); cuneus (CU); lingual (LG) and fusiform gyri (FG); retrosplenial cortex and posterior cingulate (RSC/PC); HF (hippocampal formation and parahippocampal gyrus); splenium (Sp), inferior longitudinal (ILF) and inferior-fronto-occipital fasciculus (IOF); thalamus and midbrain. The number of ischemic lesions on the list was counted. Thalamic lesions were labelled according to ([28,38]).
Table 1
Demographical and clinical data.

| Lesion Type       | Cortical lesions (n = 35) | Combined lesions (n = 31) | Thalamic lesions (n = 18) | P (Kruskal-Wallis) |
|-------------------|--------------------------|---------------------------|--------------------------|-------------------|
| Age (mean, SD)    | 68.3/14.3               | 57.9/12.8                 | 52.8/11.4                | 0.003             |
| NIHSS (mean, SD)  | 1.8/4.5                 | 4.5/2.4                   | 4.9/2.1                  | 0.000             |
| mRS (mean, SD)    | 1.8/3.2                 | 2.4/2.2                   | 2.2/1.0                  | 0.015             |
| Lesion volume pixels (mean, SD) | 22,198/13,920 | 31,600/15,345 | 1712/936 | 0.000 |
| # structures involved (mean, SD) | 7.1/2.1 | 10.2/2.2 | 1.2/0.9 | 0.000 |
| Risk factors (%)  | 80/25.7; 17.1 | 61.3/22.5; 8.6 | 50/5.5; 11.4 | – |
| Stroke etiology (%) | 51.4/31.4 | 41.9/54.8; 2.6 | 16.7/33.3; 33.3 | – |
| Visual fields (%) | 14.3/25.7; 25.8 | 19.4/51.6; 9.7 | 27.8/11.1; 25.8 | – |

Legend: NIHSS = NIH Stroke Scale, mRS = modified Rankin Scale, # structures involved = number of ischemic brain regions. Risk factors 1 = hypertension, 2 = diabetes, 3 = smoking, 4 = hyperlipemia, 5 = atrial fibrillation. Stroke etiology (TOAST), 1 = macroangiopathy, 2 = microangiopathy; 3 = cardioembolism; 4 = other determined etiology; 5 = unknown. Visual fields: 1 = normal, 2 = homonymous hemianopia, 3 = superior quadrantanopia, 4 = inferior quadrantanopia.

3. Results

3.1. Clinical characteristics

Eighty-four patients (26 females) were included. Patient data, allocation to subgroups, risk factors and the presumed etiology are summarized in Table 1.

The three groups differed significantly with regard to age, NIHSS, mRS, lesion volume and lesions characteristics (Table 1). Patients with combined lesions were younger (p < .003), had higher NIHSS scores (p < .000), higher mRS scores (p < .004) and a larger number of ischemic brain structures than in the cortical group (p < .003). Despite being the youngest participants with the smallest lesion load the thalamic lesion had the highest NIHSS scores.

The most frequent neurological findings were VFD (64.3%); 29.8% had homonymous hemianopia (combined: 52%, cortical: 26%) and 29.8% superior quadrantanopia (combined: 49%, cortical: 26%). Inferior quadrantanopia was rare (6%); 34.4% had intact visual fields. Motor signs like limb weakness, facial droop or dysarthria were found in 30%, followed by sensory signs (22.1%), impairments of consciousness (dizziness, sopor; 11.9%), cognitive deficits (aphasia, dyslexia, memory impairment; 7%), oculomotor deficits (diplopia; gaze paralysis, nystagmus, skew deviation, ocular tilt; 7.1%) and ataxia (4.8%).

Lesion subgroups differed with respect to their clinical features. VFD were only found after combined and cortical lesions, and oculomotor abnormalities only after meso-diencephalic lesions (thalamic and combined). Sensorymotor signs accumulated among combined lesions (motor: 39%; sensory: 42%) as compared to the cortical group (motor: 6%, sensory: 3%). The 3 patients with bilateral thalamic lesions presented with obtundation, tetraparesis and vertical gaze paralysis; they were clinically most impaired.

3.2. Lesion study

3.2.1. Lesion topography

Lesion topography is illustrated in Fig. 1-4.

3.2.2. Lesion anatomy

Lesion distribution and frequency is listed in Table 2.

3.2.3. Lesion subgroups

Superficial (cortico-subcortical) lesions accounted for 41.7% of all lesions. The mean number of anatomical areas with ischemia was 7.1. Ischemic lesions were frequently found in the LG, FG, GTI, IOG, and the calcarine branch territory (Cu). The RC/PC and OR, superior portion were less often involved. There were numerous lesions of white matter tracts, particularly the IFOF and ILF, less often the OR, inferior portion.

Combined lesions accounted for 36.9%. The mean number of ischemic lesions was 10.5. As in the cortical group, ischemia was mostly located in LG, FG, IOG, Cu and RC/PC. In contrast, the occurrence of temporal lesions including the HF was much higher in the combined than in the cortical group (94% vs. 17%) which is evident from both.
lesion frequency (Table 2) and the coronal overlay plots (Figs. 2, 3, y – 50 to –10). White matter tracts (IFOF, ILF, ORC, ORI) were also more often lesioned than in the cortical subgroup. By definition, all patients had thalamic lesions, with three of them extending to the midbrain (Fig. 4). Frequent lesion patterns in the thalamus were inferolateral, followed by posterior, and polar. Eleven patients in this group had lesions extending to a second thalamic territory (inferolateral + posterior: 5, inferolateral + polar: 2, polar + paramedian: 2, polar + posterior: 2).

Isolated thalamic lesions accounted for 21.4%. Lesions were all single lesions. The most frequent thalamic lesions were paramedian, followed by inferolateral and polar. Nine patients (60%) had lesion extending to the midbrain. All bilateral thalamic lesions were of the paramedian type.

3.2.4. Lesions causing VFD

Patients with VFD had lesions mostly in mesial and ventral occipital region, including the cuneus, the lingual and fusiform gyrus, the inferior and medial occipital cortex, the optic radiation (inferior > superior) and the inferior longitudinal and inferior-fronto-occipital tracts.

4. Discussion

In the setting of acute stroke a quick attribution of clinical symptoms to a vascular territory is essential and might assist in reliable treatment decisions. This study illustrates the anatomical distribution of PCA territory infarcts in a large patient sample which was separated into subgroups according to the origin of stroke. Different from previous clinico-anatomical studies which were based on visual analysis, we used spatially normalized lesions and an automated anatomical labelling procedure allowing for more objective results. Our findings confirm the hypotheses claiming a preponderance of lesions located in the ventral and mesial supply area of the PCA ([24,35] with a maximum of lesion frequency on the X-Y-Z slices –20, –70, –5, while parieto-occipital and

Fig. 2. Lesion overlay plot of cortical group, coronal cuts.

Fig. 3. Lesion overlay plot of combined group, coronal cuts.
dorsal areas were rarely involved. The observed lesion pattern was similar in both hemispheres. A further issue regards lesions of white matter tracts. Previous studies proposed that white matter bundles connecting the occipital and parietal lobe with more anterior brain regions support cognitive functions such as visual perception, recognition of objects, faces and places, reading, object identification and naming, as well as episodic and semantic memory ([9,14,22,23,29,30,40]. Due to their location, the OR, long posterior-anterior association tracts and commissural connections were among the most often damaged structures in our cohort. This indicates that patients with PCA stroke may be endangered to lose important cognitive capacities via disconnection of fibre tracts. It also suggests that lesion studies of PCA stroke may be of interest to further examine the clinical correlates of white matter lesions.

The findings of our study are capable to explain several clinical features of PCA stroke, e.g. the frequent occurrence of homonymous hemianopia and superior quadrantanopia, whereas inferior quadrantanopia was rare. Reasons for this dissociation are the dominance of ventral and medial lesions and the fact that the superior OR is partly supplied by the MCA [11]. In addition to calcarine and OR lesions, PCA stroke is often associated with a disruption of the ventral visual stream [20] causing deficits of higher order visual processing, such asagnosia, alexia, achromatopsia or lexico-semantic deficits ([5,7,17,31,35]. PCA stroke may also produce spatial neglect due to affection of the perisylvian brain network at the border zone between the PCA and MCA territories [41]. Further, disorders of memory and learning may occur as a consequence of damage to the mesial temporal lobe memory system [47]. The true prevalence of cognitive impairments after acute PCA stroke is remains unclear, since they are rarely reported by patients and seldom assessed in stroke studies. It is neither reflected in our study as patients were assessed in the setting of acute stroke where more obvious neurological deficits are searched and registered during assessment.

An important finding is that the subgroups of acute PCA infarcts differ as to demographical and clinical characteristics. Patients with combined lesions (including cortex, white matter and thalamus) were younger, clinically more impaired (including VFD), had larger lesion volumes, a larger number of ischemic regions than patients of the cortical lesion type; furthermore, ischemia included the mesiotemporal and hippocampal region more often. In contrast, patients with cortical (superficial) lesions were older and clinically less impaired, had smaller lesion volumes, a lower number of ischemic regions and a lower prevalence of VFD. In view of these findings and with reference to the acute phase, combined lesions represent a more pronounced PCA stroke variant with more serious consequences than cortical lesions; moreover, patients with isolated thalamic, particularly those with bilateral lesions, were the youngest and had the utmost clinical impairment, despite their circumscribed, mostly lacunar lesion. Clinically, they had no VFD, whereas oculomotor signs, ataxia and somnolence were frequent. This suggests that the distinction according to lesion levels is useful to diagnose and study ischemic PCA stroke. Future studies with larger patient samples will be necessary to confirm this hypothesis.

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