

# The human pyramidal syndrome Redux

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Received 11 May 2007; accepted 7 June 2007

Experimental studies in nonhuman primates have questioned the selectivity of pyramidal tract damage in giving rise to the classical pyramidal syndrome in humans, characterized by permanent spastic hemiplegia (PSH). According to this view, concomitant injury of extrapyramidal pathways is necessary for the development of both hemiplegia and spasticity. In this study we used conventional magnetic resonance imaging and diffusion tensor imaging tractography

to characterize the anatomical correlates of PSH in a patient with a rare and discrete unilateral lesion of the medullary pyramid. Our findings support the hypothesis that damage confined to the medullary pyramid/pyramidal tract is sufficient to produce PSH. In contrast to nonhuman primates, the human 'pyramidal' and 'pyramid' syndromes are equivalent clinico-anatomic concepts. *NeuroReport* 18:1417–1421 © 2007 Lippincott Williams & Wilkins.

**Keywords:** medullary pyramid, pyramidal tract, spastic hemiplegia, tractography

## Introduction

The exact anatomical correlates of permanent spastic hemiplegia (PSH) were hotly debated throughout the twentieth century. The early tenet that PSH resulted from degeneration, focal damage, or dysfunction of the contralateral pyramidal tract (PT) was challenged by experimental evidence [1] that implied that PSH would only occur if extrapyramidal pathways, the collection of descending supraspinal motor pathways that reach the cord following a tegmental course [2], were concomitantly injured [3]. As the medullary pyramids are the only place in the nervous system where the PTs are entirely isolated, lesions therein confined are ideally suited to test the idea that a pyramid lesion suffices to produce PSH. Discrete pyramid lesions in man, however, are rare, and when they do occur, patients usually survive them for years, adding to the scarcity of correlative necropsy material. This study draws upon the new MRI techniques of diffusion tensor imaging (DTI) and tractography to investigate the rare case of a patient with PSH caused by a unilateral and capriciously localized infarct of the left medullary pyramid. Our main goal was to revisit the hypothesis that injury of one pyramid suffices to produce the classical pyramidal syndrome in humans. To illustrate further the specificity of our findings, we studied three additional patients with PSH harboring less selective, more proximal lesions of the motor pathway, as well as four normal healthy volunteers.

## Report of case (patient M.P.): unilateral damage to the medullary pyramid

M.P., a 62-year-old man, presented in a wheelchair in December 2001 complaining of right-side weakness which

struck him the night before as he went to bed. He was awake and oriented, and could speak, swallow, and move his face normally. His right arm and leg were motionless, but he denied tingling or pins-and-needles sensations. One week later, he could stand up and walk unsupported again. In one month, he had developed a typical hemiplegic attitude, most evident as he stood and walked. On walking, he circumducted the right arm and leg, but did not scuff the toes on the ground. No Romberg sign was observed and the postural adjustments to sudden postural imbalances were normal. Vertical and horizontal pursuit and saccadic eye movements were normal and without nystagmus. The face was symmetric at rest, as well as when he talked and smiled. The tongue was symmetric at rest and on protrusion. Tendon jerks were hyperactive, with ankle clonus and a Hoffmann sign on the right. The plantar reflex was extensor on the right and flexor on the left. His visual fields were full and the corneal reflexes were intact. A characteristic distribution of weakness was noted on arm abduction (4/5), forearm extension (4/5), and hand/fingers flexion (3/5) and extension (0/5). Weakness in the lower limb was observed on thigh flexion (4/5), leg extension (4/5) and flexion (3/5), and in plantar extension (1/5) and dorsiflexion (3/5) of the foot. Spasticity also adopted a characteristic distribution, being most evident in the arm and wrist flexors (5/5), and in the leg flexors and extensors (4/5). Sensation to pinprick, light touch, position sense, and vibration (128 Hz tuning fork) were normal and symmetric all over the body, including the face. His handedness shifted from a pre-morbid +80 to a current -20 on the Edinburgh Inventory. He scored 28/30 on the mini-mental state examination (MMSE) [4] and 85/100 on the Barthel index, due to bladder incontinence and the inability to climb stairs unaided.

## Materials and methods

### Patients

In addition to the patient described above (M.P.), three additional patients with PSH and four healthy individuals were included for comparison (pathologic and normal controls). B.P. was densely hemiplegic due to a left ventral pontine infarct, from which she recovered in a few weeks. C.R. and M.C.A. presented with a PSH due to a supracapsular ischemic lesion—in the right corona radiata (C.R.) and in the cortico-subcortical territory of the left middle cerebral artery (M.C.A.) respectively. All participants gave written informed consent before entering the study, which was approved by the LABS-D'Or institutional review board.

### Neurobehavioral assessment

Somatic sensibility was probed by a set of tests designed to assess its finer aspects: replication of passive manual attitudes of the contralateral hand with the eyes open and closed [5], thumb localization [6], direction of scratch [7], tactile form perception [8], finger localization [8], Weber's two-point discrimination [9], moving two-point discrimination [10], and determination of sensory thresholds of finger tips [9]. Motor strength, spasticity, and tendon reflexes were graded respectively with the Medical Research Council [11], the modified Ashworth [12], and the National Institute of Neurological Disorders and Stroke (NINDS) scales [13]. M.C.A. was unable to cooperate because of global aphasia.

### Neuroimaging

Anatomical images were obtained with T1 spin-echo, T2 turbo spin-echo and FLAIR pulse sequences in a 1.5-T Philips-Intera scanner (Eindhoven, The Netherlands). Diffusion-weighted images were acquired with a single-shot, spin-echo echoplanar sequence: TR/TE=4000/110, field-of-view=256 mm<sup>2</sup>, matrix=112 × 128, slice thickness=5 mm without gap. Diffusion sensitization gradients were applied in six noncollinear directions, with a *b* factor of 800 s/mm<sup>2</sup>. DTI was transferred and postprocessed using Philips Research Integrated Development Environment software (PRIDE research platform, Fiber Track 4.1, Eindhoven, The Netherlands). Fractional anisotropy (FA) maps color-coded for direction, and fiber-tracking calculations were performed by specifying regions-of-interest (ROIs) on the trajectory of the PT in the cerebral hemisphere and ventral brainstem [14] at (i) the pontomedullary transition, (ii) the middle third of the cerebral peduncle, and (iii) the posterior limb of the internal capsule. Automatic tracking of fibers was performed with a marching algorithm restricting fiber

tracking to voxels with a minimum FA of 0.30. Fiber deflection threshold was set to 0.85. In patients, the normal side was also used as a control for the results of tractography.

### Statistical analysis

To assess the discrepancy between intraindividual measures of homologous ROIs in each hemisphere we compared the FA values of patients with those of the healthy volunteers. The significance of intraindividual differences for each pair of ROIs was assessed with a modified paired samples *t*-test [15], adopting a threshold of significance ( $\alpha$ ) of 0.05, two-tailed. In contrast to earlier statistical techniques, the modified *t*-test employed here does not overestimate the rarity of differences when control data are derived from small samples. These considerations become especially important in situations where the two measures of interest are highly correlated (in this case, the left and right FA values), an occurrence that often induces clinicians to dismiss discrepancies as 'modest', but which are, in fact, highly abnormal.

**Table 2** Summary of clinical and behavioral findings

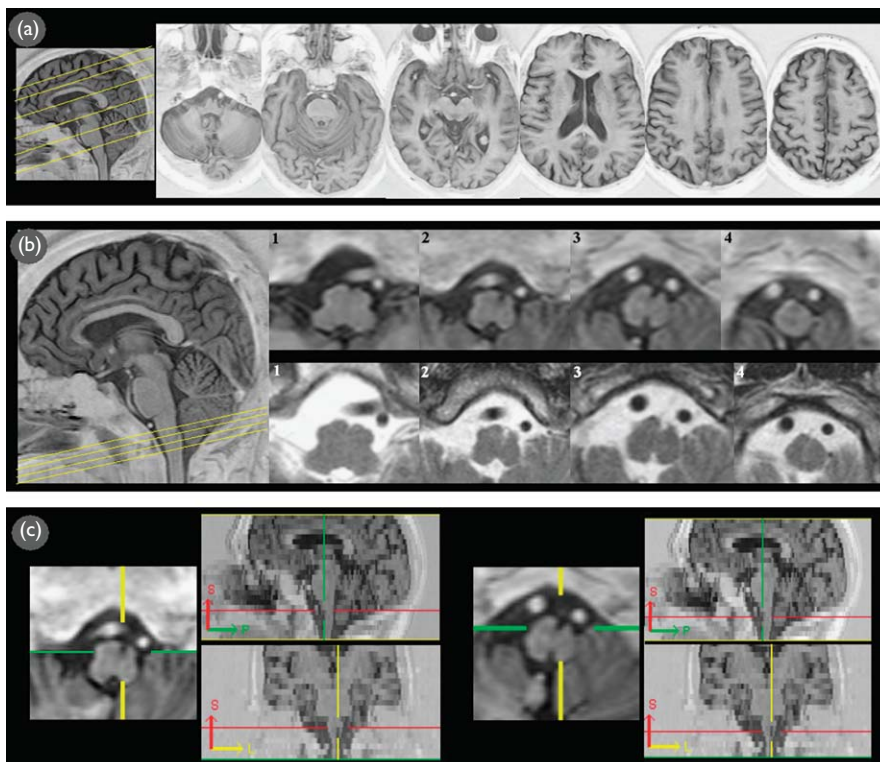
Tests	M.P.	B.P.	C.R.	M.C.A.
Sensory exam				
Two-point discrimination threshold (mm)				
Right index finger	3	—	—	—
Left index finger	3	—	—	—
Moving two-point discrimination threshold (mm)				
Right index finger	2	—	—	—
Left index finger	2	—	—	—
Direction of scratch test				
Face (cheek)				
Right (0–10)	10/10	10/10	10/10	—
Left (0–10)	10/10	10/10	10/10	—
Hand (palmar surface)				
Right (0–10)	10/10	10/10	10/10	—
Left (0–10)	10/10	10/10	10/10	—
Tactile form perception				
Left hand (0–10)	10/10	10/10	10/10	—
Right hand (0–10)	08/10	08/10	8/10	—
Finger localization test				
Single fingers				
Left hand (0–10)	10/10	10/10	10/10	—
Right hand (0–10)	10/10	10/10	10/10	—
Pairs of fingers				
Left hand (0–10)	10/10	9/10	9/10	—
Right hand (0–10)	10/10	9/10	9/10	—
Sen. Ind. fingertip (g) (0.008–0.08)				
Left	0.080	—	—	—
Right	0.080	—	—	—
Thumb localizing				
Left (0–3)	3	3	—	—
Right (0–3)	3	3	—	—
MMSE (0–30)	28	30	29	0
Barthel index (0–100)	85	95	30	30
Ed. Hand. Invent. (–100/+100)				
Premorbid	80	100	100	100
Current	–20	100	100	–100

Ed. Hand. Invent. (–100/+100), Edinburgh Handedness Inventory (range: –100/+100); MMSE, mini-mental state examination; Sen. Ind. fingertip (g) (0.008–0.08), Sensory thresholds in index fingertip (g) (normal range: 0.008–0.080).

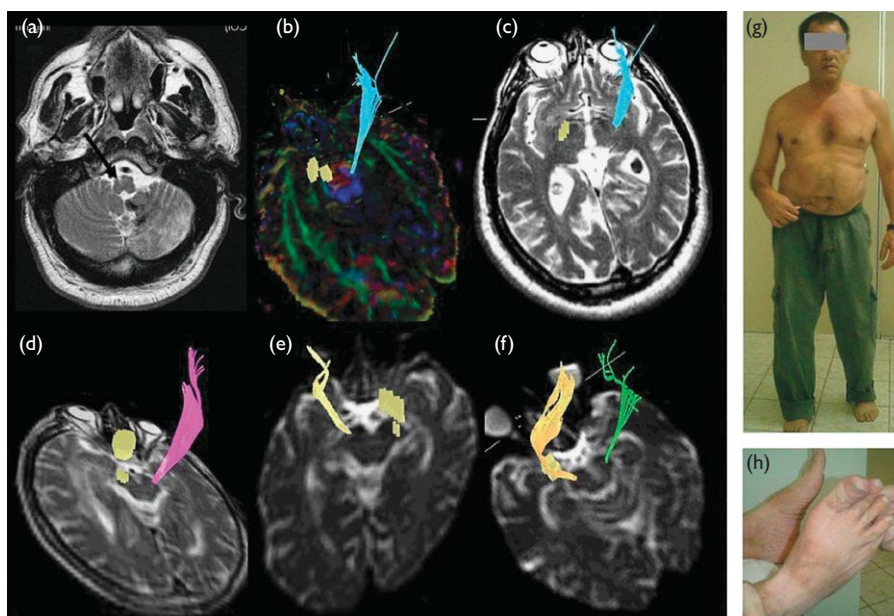
**Table 1** Patient demographics and clinical characteristics at the acute/subacute phase, and examination at chronic stage

Characteristics	M.P.	B.P.	C.R.	M.C.A.
Sex	Man	Woman	Woman	Man
Age (years)	62	71	71	77
Acute/subacute	R-Hp	L-Hp	R-Hp	L-Hp + global aphasia
Chronic	L-PSH	Recovered	L-PSH	R-PSH

L-Hp, left hemiplegia; L-PSH, left permanent spastic hemiplegia; R-Hp, right hemiplegia; R-PSH, right permanent spastic hemiplegia.



**Fig. 1** (a) T1-weighted, inversion-recovery (TIW-IR) MRI images of M.P. at different levels across the lower brainstem and cerebral hemispheres. No significant abnormalities were observed at these levels. (b) Zoomed views of medullary pyramid lesion of M.P. The sagittal image shows the location of transverse cuts across the medulla oblongata (TIW-IR and T2-weighted images are displayed in the superior and inferior rows respectively, from dorsal to ventral levels). A small infarct at the level of the left medullary pyramid can be clearly observed as a wedge-shaped hypointensity in TIW images and hyperintensity in T2W images (slices 2 and 3). Note that slices 1 and 4, located 5 mm above and below the lesion, do not show abnormalities. (c) Reformatted TIW-IR images of the medullary pyramid lesion of M.P. Note the fusiform shape of the lesion, best appreciated in the coronal views.



**Fig. 2** (a) The left medullary pyramid infarct is shown on an axial T2 weighted image (T2WI) in M.P.; (b–f) fiber-tracking results from the three regions-of-interest approach. (b, c) Normal appearance of the reconstructed right PT and its absence in the left hemisphere in color-coded FA map (b) and T2WI (c) of M.P. (d) Intact PT in the right hemisphere and its absence in the left hemisphere in M.C.A. (e) Normal appearance of the reconstructed left PT and its absence in the right hemisphere in C.R. (f) Normal appearance of the reconstructed left PT and decrease in bulk on the right PT in B.P. (g and h) Typical Wernicke–Mann hemiplegic attitude during walking and right extensor plantar reflex in M.P. PT, pyramidal tract.

## Results

### Clinical and behavioral findings

The main clinical and behavioral findings are summarized in Tables 1 and 2.

### Neuroanatomical findings

M.P. had a T1-hypointense/T2-hyperintense spindle-shaped lesion in the left ventromedial medulla well above the pyramidal decussation. The lesion was confined to the pyramid, with its major length paralleling the longitudinal axis of the brainstem, leaving the tegmentum and the medial lemnisci intact (Figs 1 and 2a). It corresponded to the type-2 infarction of Katoh and Kawamoto's classification [16], indicating that the anatomical boundaries of the medullary pyramid had not been exceeded. Such infarcts usually result from occlusion of a median perforating branch of the vertebral artery [17]. B.P. had an infarct occupying the lower third of the right basis pontis that rendered her hemiplegic for a few weeks. The infarct fell within the territory of the anterolateral pontine arteries, which supply the ventrolateral pontine base, including the lateral portions of the PT [18]. C.R. and M.C.A. developed a disabling PSH from which there was little recovery: in C.R. a small infarct was seen in the corona radiata underneath the right precentral cortex, whereas M.C.A. suffered an extensive infarct of probable embolic origin occupying the superficial and deep territories of the left middle cerebral artery.

### Diffusion tensor imaging and tractography findings

In comparison with the normal side, FA was decreased at and below the site of damage in all patients (Table 3). This corresponds respectively to local effects (at lesion level) and to Wallerian degeneration [19]. FA values rostral to the injury were normal in both patients with ventrocaudal brainstem lesions (M.P. and B.P.). The intact PT was reconstructed from the medullary pyramid to the subcortical rolandic region in all patients. On the injured side, the PT was not visible in the three patients with PSH (Fig. 2b–e). In B.P., who recovered from hemiplegia, the PT on the side of injury was clearly seen, although diminished in bulk

(Fig. 1f). Figure 1g and h depict the patient's spastic hemiplegia and the extensor plantar reflex.

## Discussion

This study investigates a patient with a rare, selective lesion to the left medullary pyramid who developed PSH. MRI and tractography confirmed the damage to the PT and the preservation of neighboring structures. The discreteness of the pyramid lesion was further attested by the sparing of somatic sensibility (medial lemnisci), by the preservation of facial (corticofacial fibers) and lingual (hypoglossal nucleus and nerve) motility, as well as by the absence of vertical nystagmus (medial longitudinal fasciculus). The neuroimaging findings in the additional patients with PSH (M.P., C.R., and M.C.A.) showed patterns compatible with a more widespread, less selective Wallerian degeneration of cortico-spinal and cortico-bulbar tracts. Moreover, the remaining PT fibers caudal to the pons observed in patient B.P. probably accounted for her good recovery [20,21]. In conclusion, our findings substantiate *post-mortem* observations that, in contrast to the nonhuman primate, a unilateral infarct confined to the medullary pyramid suffices to produce contralateral PSH in humans [22–25].

## Acknowledgements

The authors are indebted to Mr José Ricardo Pinheiro and Mr Jorge Baçal (Section of Rare Documents and Works, Instituto Oswaldo Cruz Library, Rio de Janeiro) for the retrieved classical journal articles and books.

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**Table 3** Fractional anisotropy values along the pyramidal tract of patients and healthy controls

	Ponto-medullary (left/right)	Cerebral peduncle (left/right)	Internal capsule (left/right)
Controls			
1	0.47/0.51	0.72/0.68	0.60/0.61
2	0.58/0.59	0.78/0.75	0.64/0.62
3	0.55/0.57	0.75/0.75	0.60/0.56
4	0.56/0.59	0.82/0.80	0.71/0.68
Patients			
MP	0.46*/0.69	0.57/0.60	0.61/0.59
BP	0.58/0.21*	0.66/0.64	0.70/0.70
CR	0.54/0.39*	0.66/0.45*	0.60/0.49*
MCA	0.26*/0.52	0.48*/0.75	0.25*/0.68

Regions-of-interest (ROIs) placed in left and right cerebral hemisphere and ventral brainstem at: (i) the ponto-medullary transition, (ii) the middle third of the cerebral peduncle, and (iii) the posterior limb of the internal capsule.

\* $P \leq 0.001$ , two-tailed (following the modified paired samples t-test procedure of Crawford *et al.*, 1998) [15].

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