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### Midbrain Ataxia: Possible Role of the Pedunculopontine Nucleus in Human Locomotion

Roongroj Bhidayasiri<sup>a</sup>, Gasser Hathout<sup>b</sup>, Stanley N. Cohen<sup>a</sup>, Wallace W. Tourtellotte<sup>a</sup>

Departments of <sup>a</sup> Neurology and <sup>b</sup> Radiology, Veterans Affairs West Angeles Healthcare Center and UCLA Medical Center, UCLA School of Medicine, Los Angeles, Calif., USA

Midbrain lesions have rarely been implicated as a responsible location in patients presenting with gait instability. In animals, stimulation of the pontomesencephalic area results in rapid walking followed by running. Ablative lesions in this area cause a reduction of locomotor activity [1]. However, the center in humans is probably more dependent upon cortical and subcortical input to activate the system. We report a case of a 66-year-old male who had a subacute infarction in the left posterior tegmentum presenting primarily with gait instability, further supporting the evidence that brainstem locomotor regions also exist in humans.

### Case Report

A 66-year-old man with a known history of poorly controlled diabetes and hypertension presented to the emergency room with complaints of a sudden onset of unsteadiness and blurred vision. On examination, his blood pressure was 176/95 with regular pulse rate at 76 per minute. Eye movement examination showed restricted up gaze more than down gaze, impaired convergence and skew deviation of the eyes in the primary position with the left being hypertrophic by about 20 degrees. No nystagmus, lid lag or pupillary abnormalities were observed. Coordination testing revealed intact fingerto-nose and heel-to-shin tests. Station and gait testing was significant for severe truncal ataxia. The patient was able to stand from a chair, with a wide base. He generated short irregular steps, which were of variable amplitudes and directions, sometimes directed laterally, lacking rhythmicity. He was not able to perform tandem gait. Deep tendon reflexes were symmetrical and both plantar responses were flexor. There was no lateralizing sensory deficit. Repeated examination 3 days later showed significant gait improvement; however, the eye findings remained unchanged. On fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted magnetic resonance imaging performed in relation to symptom onset, there was a 3-mm focus of increased signal intensity in the left posterior tegmentum of the rostral mesencephalon, anterior to the sylvian aqueduct and dorsal to the left red nucleus, consistent with subacute small infarct (fig. 1). In addition, there were a few scattered punctate foci of increased signal intensity in the periventricular white matter on FLAIR and T2-

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**Fig. 1.** Magnetic resonance imaging scans (1.5 T). Axial image. FLAIR magnetic resonance imaging showed a 3-mm focus of increased signal intensity in the left posterior tegmentum of the rostral mesencephalon, anterior to the sylvian aqueduct and dorsal to the left red nucleus, consistent with subacute small infarction.

weighted images. No lesions were seen in the thalamus or cerebellum. Magnetic resonance arteriogram of the neck and intracranial vessels was unremarkable.

### Discussion

Our patient had a lesion involving the left posterior tegmentum of the midbrain, which most likely damages the following structures: accessory oculomotor nuclei, mesencephalic tegmental tract, dentatorubrothalamic tract and mesencephalic reticular formation. The most likely etiology of this infarction is small-vessel disease, related to a history of poorly controlled diabetes and hypertension. The functionally defined mesencephalic locomotor region containing the pedunculopontine nucleus (PPN) is located in the mesencephalic reticular formation. In humans, the PPN is bound on its lateral side by the medial lemniscus fibers and on its medial side by fibers of the superior cerebellar peduncle. Rostrally, the PPN contacts the dorsomedial aspect of substantia nigra and the retrorubral field [2]. The most caudal pole of the PPN is adjacent to the locus ceruleus (fig. 2) [2]. Our patient's vertical gaze palsy, skew deviation and impaired



**Fig. 2.** Sagittal view of a human brainstem showing the location of different nuclei. Dotted areas mark the location of the PPN. III = Oculomotor nucleus; IV = trochlear nucleus; VI = abducens nucleus; IC = interstitial nucleus of Cajal; IO = inferior olive; LC = locus ceruleus; riMLF = rostral interstitial nucleus of medial longitudinal fasiculus; RN = red nucleus; MB = mammillary body; SN = substantia nigra (modified by Horn et al. [11]).

convergence can be explained by the involvement of vertical and vergence gaze control in the midbrain [3]. The origin of the gait abnormality with a midbrain lesion in this location is less clear.

Despite considerable animal data available, little is known of the function of the PPN in humans or to what extent observations in experimental animals are relevant to humans. Its connectivity suggests an important role in motor behavior [1]. PPN receives afferents from deep cerebellar nuclei, substantia nigra, globus pallidus, cerebral cortex and spinal cord and projects to the contralateral substantia nigra, subthalamic nucleus, globus pallidus and thalamic nuclei [1, 2]. The potential role of PPN is probably as a relay station, providing feedback information important for the modulation of posture and gait initiation, facilitated by its prominent cholinergic ascending projections to the thalamus and its connections with deep cerebellar nuclei [2]. There is supporting evidence from neuropathological studies on humans demonstrating a significant loss of cholinergic neurons within the lateral part of the PPN pars compacta in individuals with

progressive supranuclear palsy, idiopathic Parkinson's disease and combined Parkinson's and Alzheimer's disease [4, 5]. However, on a clinical level, there has been a single case report by Masdeu et al. [6] suggesting the involvement of the PPN in human locomotion. They described the inability to stand and generate stepping movements in an 83-year-old woman with a hemorrhage at the pontomesencephalic junction involving the right pedunculopontine area. However, our patient's gait is somewhat different with severe truncal ataxia and typically wide-based gait as well as difficulty in gait initiation. The difference could be due to the disruption of pathway from deep cerebellar nuclei, superior cerebellar peduncle or crossed dentatorubrothalamic tract. Also, it is known that a main output of the locomotor regions is via the medullary reticulospinal tract, which transverses the medial ventral spinal cord. Lesions of this tract have been shown to impair locomotion and to cause imbalance [7, 8]. Incoordination of movements and truncal instability resembling cerebellar ataxia may be seen in patients with thalamic lesions, especially the superoposterolateral portion [9]. Gait ataxia without limb ataxia can also be seen in superior cerebellar artery territory infarction [10]. However, there was no thalamic lesion demonstrated in our case.

As suggested in animal studies, this case illustrates the importance of brainstem control of locomotion, particularly the PPN. It supports other evidence that this structure and its environs in humans are involved in the initiation, and modulation of gait and stereotyped movements. We would like to emphasize the mesencephalic locomotor region in the midbrain as a potential localization for a lesion in patients presenting with gait problems. Accompanied eye movement abnormalities, especially vertical gaze palsy are the clues to this lesion localization.

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R. Bhidayasiri, MD, MRCP, Department of Neurology UCLA Medical Center, 710 Westwood Plaza Los Angeles, CA 90095 (USA) Tel. +1 310 206 6766, Fax +1 310 202 0657, E-Mail rbh@ucla.edu

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