The Crossed Paralyses

The Original Brain-Stem Syndromes of Millard-Gubler, Foville, Weber, and Raymond-Cestan

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In this article, the crossed syndromes of Millard-Gubler (facial palsy and contralateral hemiparesis), Foville (facial palsy, conjugate gaze paralysis, and contralateral hemiparesis), Weber (oculomotor palsy and contralateral hemiparesis), and Raymond-Cestan (internuclear ophthalmoplegia and contralateral hemiparesis) are detailed from the original reports. These and other related syndromes were instrumental in establishing important principles in brain-stem localization: the occurrence of cranial nerve palsies contralateral to hemibody motor or sensory disturbances, the concepts of the medial longitudinal fasciculus and conjugate gaze, and the corticobulbar innervation of the facial nerve nucleus. (Arch Neurol. 1995;52:635-638)

In the mid-19th century, Millard, Gubler, and Weber described their classical brain-stem syndromes that featured cranial nerve findings contralateral to limb weakness (crossed paralyses). Their observations were harbingers for a plethora of new variations described and rediscovered during the next 100 years. The hemiplegies alternes of the protubérance annulaire (the crossed hemiplegias of thepons) were elaborated on largely by the French school of neurologists.

In this article, the original French and English literature of the crossed paralytic syndromes is revisited. The eponymous syndromes described by Millard and Gubler, Foville, Weber, and Raymond and Cestan are detailed to determine their initial components and their contributions to the understanding of brain-stem neuroanatomy.

MILLARD-GUBLER SYNDROME
(1856)

Auguste Millard (1830-1915) first proposed to the Société Anatomique of Paris (France) that “direct facial hemiplegia” accompanied by contralateral hemiplegia was a sign of pontine hemorrhage. He described a patient of Poisson’s with these findings1 and cited another case reported by Sénac of a fruit and vegetable merchant whose autopsy revealed a 5-mm midpontine area of bluish-black softening that contained an “almond-sized” hemorrhagic center.

Adolphe Gubler (1821-1897) described six additional cases and reviewed pontine neuroanatomy, including the purported evidence for decussation of the facial motor fibers.2 Gubler’s first patient was a woman with pulmonary tuberculosis, a right hemiparesis, and left facial weakness. Autopsy revealed a firm mass about the size of “a husked filbert” (12 to 15 mm in diameter) that invaded both sides of thepons but destroyed more of the left side. The seventh-nerve fibers emerging from thepons were “little if at all impaired.”2 His other cases were similar, including one first reported by Grenet of a 34-year-old man with left facial paralysis and anesthesia associated with right hemiparesis and hemianesthesia (Table).2

Gubler localized his crossed hemiplegias to thepons by considering that two lesions could individually impair the limbs on one side and the face on the other, but reasoned that a single lesion would be more parsimonious. He viewed preservation of intelligence as evidence for intact
The Eponymic Syndromes With Crossed Paralysis*

<table>
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<tr>
<th>Syndrome</th>
<th>Lesion Site</th>
<th>Clinical Syndrome</th>
<th>Original Cause</th>
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<tr>
<td>Millard-Gubler, 1856*</td>
<td>Caudal ventral pons: CN-VII; CST</td>
<td>Facial palsy; CL hemiparesis</td>
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<tr>
<td>Foville, 1858†</td>
<td>Caudal tegmental pons: CN-VII; CN-V/PPRF; CST</td>
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<td>Weber, 1863‡</td>
<td>Cerebral peduncle: CN-II; CST</td>
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<td>Raymond-Cestan, 1903§</td>
<td>Rostral tegmental pons: MLF; CST, ML, STT, SMCP</td>
<td>INO; CL dyesthesias, cerebellar signs, hemiparesis</td>
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<td>Grenet, 1855§</td>
<td>Middle tegmental pons: CN-V, SCP; STT, CST</td>
<td>Facial anesthesia, paralysis of muscles of mastication, ataxia, tremor; CL anesthetia, hemiparesis</td>
<td>Tumor</td>
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<tr>
<td>Benedikt, 1889**10</td>
<td>Cerebral peduncle: CN-III; CST, SN, RN?</td>
<td>Oculomotor palsy; CL hemiparesis; tremor, involuntary movements</td>
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<td>Raymond, 1896¶</td>
<td>Caudal ventral pons: CN-VII; CST</td>
<td>Lateral rectus palsy; CL hemiparesis</td>
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<td>Gelli, 1901**12</td>
<td>Caudal ventral lateral pons: CN-VII = CN-VII; CST</td>
<td>Deafness, hypoaesthesia, buzzing, vertigo; ear ache = facial palsy; CL hemiparesis</td>
<td>?</td>
</tr>
<tr>
<td>Brissaud and Sicard, 1908¹</td>
<td>Caudal ventral pons: CN-VII; CST</td>
<td>Facial hemiparesia; CL hemiparesis</td>
<td>Syphilis</td>
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<tr>
<td>Marie-Fox, 1913**4</td>
<td>Rostral lateral pons: MCP; CST</td>
<td>Cerebellar signs (eg, ataxia); CL hemiplegia</td>
<td>Syphilis</td>
</tr>
</tbody>
</table>

* CL indicates contralateral; CN, cranial nerve; CST, corticospinal tract; MLF, medial longitudinal fasciculus; INO, internuclear ophthalmoplegia; PPRF, paramedian pontine reticular formation; question mark, postulated or not reported; ML, medial lemniscus; STT, spinothalamic tract; SMCP, superior/middle cerebellar peduncle; SN, substantia nigra; RN, red nucleus; and plus or minus sign, with or without.

cerebral hemisphere function. Contralateral paralysis of the limbs was consistent with the view that the pyramidal tracts decussated caudally within the medulla.

Finally, Gubler apparently believed that nerve fibers, originating in the contralateral cerebral hemisphere and completely crossing in the brain stem without synapsing, were responsible for facial movements. Hence, lesions above this decussation resulted in a contralateral facial paralysis, while those more caudal (i.e., in the pons) caused an ipsilateral palsy. He offered his first case,† with an extra-axial lesion and the extra-axial facial nerve “seeming nearly sound,” as supporting evidence for the pontine localization of his symptom complex. The facial palsy in this patient likely resulted from a lesion of the facial nucleus or fascicle. Gubler failed to understand the unique bilateral supranuclear innervation of the facial nerve nucleus.³

In an addendum* to Gubler’s article,² Millard requested that his two cases¹ be reprinted, for he agreed with Gubler that “crossed facial hemiplegia” was a sign of pontine lesions. An attached editor’s note indicated that Gubler had acknowledged Millard as the first to recognize a possible relationship between “direct facial hemiplegia” and pontine lesions. This admission and Millard’s correspondence⁴ explain the attachment of Millard’s name to Gubler’s.¹ In 1893, Charcot referred to the inferior pontine crossed paralysis as la paralysie alterne de Gubler, but he also recognized that Millard’s discovery, having occurred “at the same time,” justified the eponymous use of both names.⁵

The original patients of Millard and Gubler did not have sixth nerve palsies, and their lesions in the caudal ventral pons probably affected the corticospinal tract and seventh nerve fascicle. However, later descriptions of their syndrome by Raymond and Cestan⁶ included ipsilateral abduption deficits and “internal strabismus.”

FOVILLE’S SYNDROME (1858)

Achille Louis Foville (1799-1878) described a 43-year-old commissionaire with right-sided weakness, total left facial paralysis, and an inability to look leftward: “while he tries to move both or each separately, the eyes at once appear in the middle of the interpalpebral space to stop without being able to pass over.”⁷

In an attempt to understand his patient’s conjugate gaze palsy, Foville likened the control of horizontal conjugate eye movements to a man steering two horses by uniting the reins in each hand.⁷ Similarly, each side of the pons would send its own fibers, traveling to both the ipsilateral abductor and, by decussation, the contralateral adductor. Hence, though Foville lacked pathologic findings to support any localization for his patient’s lesion, he reasoned that the clinical findings alone could be explained by a unilateral pontine lesion. His patient most likely had a lesion similar to that described by Millard and Gubler with dorsal extension into the pontine tegmentum damaging either the sixth-nerve or the paramedian pontine reticular formation. Foville⁷ also proposed that a similar arrangement existed between the “great oblique” muscle on one side and the “small oblique” muscle on the other side to explain the ocular adjustment during head tilt.

In 1900, Grasset⁶ criticized Raymond’s contention that the paralysis of conjugate gaze was, in fact, simply a paralysis of the lateral rectus muscle. Grasset, citing work by Parinaud and Graux, countered that abducens palsy and conjugate gaze paralysis were distinct entities caused by separate lesions; while the impairment of abduction alone was due to disruption of the sixth cranial nerve at its emergence from the pons, paralysis of conjugate gaze func-
tion was secondary to a lesion of its nucleus.8

WEBER'S SYNDROME (1863)

In 1863, Hermann Weber (1823-1918), a physician at the German Hospital in London (England), first presented a 52-year-old man with a right hemiparesis and left oculomotor palsy caused by a hemorrhage into the left cerebral peduncle.3 The patient had right facial weakness, right tongue deviation, left upper eyelid ptosis, and left pupillary mydriasis. The left eye was exodeviated with intact abduction and intorsion. Sensory testing, measured with Sieveking's aesthesiometer, found two-point discrimination to be diminished in the right aspect of the face and body.

His patient died 2 months later of bronchopneumonia and pleuritis. Postmortem examination3 revealed "several atheromatous spots" in the intracerebral internal carotid artery, basilar artery, and the left middle and posterior cerebral arteries. The left cerebral peduncle appeared slightly fuller than the right and contained an "oblent clot of blood" approximately 15.0 X 6.3 mm in the "internal half" of "the center of the lower part of the crus." The left third nerve fibers were "scanty and broken down," with "oil globules and granules" and "small granular corpuscles."

Weber immediately recognized that this case belonged in the category of his French colleagues' paralysis alterne. He attributed the syndrome to "any considerable lesion of the centre, the internal and lower portions of the crus cerebri." He listed the findings from such a lesion as: ipsilateral oculomotor palsy, near complete contralateral weakness of limbs, transitory contralateral facial palsy, impairment of contralateral "pneumogastric and sympathetic nerves," a "great retardation in the functions of the intestinal canal," and "immunity of the intellectual faculties."10

According to Grasset,8 in 1881, Charcot established the eponym of the pédonculaire syndrome in Weber's honor, but work by D'Astros from 1894 established that Gubler had, in fact, described this syndrome first, "four years before Weber." After examining the cases of Koechlin and Luton, Gubler suggested that from "a motor paralys of the left 'common ocular' with a total right hemiplegia" one would diagnose a lesion of the left cerebral peduncle.8 Hence, Grasset referred to the symptomatology of a lesion to the "superior part of the pons" as the syndrome Gubler-Weber.

RAYMOND-CESTAN SYNDROME (1903)

During his grand rounds in early 1895, Fulgence Raymond (1844-1910), Charcot's successor as professor of the clinique des maladies nerveuses de la Salpêtrière (Paris, France), described a syphilitic woman with left abducens impairment and contralateral hemiparesis.3 In this description of the syndrome that bears his name (Table), Raymond theorized that a lesion of the lower pons could damage both the pyramidal tract and the abducens nerve but spare the more lateral facial nerve. Unfortunately, Raymond's patient apparently had other lesions, because a right facial paralysis, aphasia, and difficulty recognizing her husband's face preceded her diplopia.5

Raymond's lecture5 showed a more advanced understanding of the neuroanatomy than the earlier work of Gubler2 and Foville.7 For example, though yet to be named, the medial longitudinal fasciculus was no longer hypothetical, its existence confirmed by the work of Duval and Laborde (cited by Raymond and Cestan). Raymond also understood in great detail the structure of the cerebral peduncle and, unlike Gubler, was aware of the pathway of the corticobulbar fibers from the motor cortex through the genu of the internal capsule to their decussation in the pons and their innervation of the facial-nerve nucleus.3

Between January 1901 and July 1903, Raymond and the head of the clinic at the Salpêtrière, Cestan (1872-1934), collected three cases6 suggestive of a syndrome, which, like Foville's, included deficits of horizontal eye movements. The authors described the eyes as being unable to attain the "external angle"; the abducting eye on the side of the lesion displayed "jerks of paralytic nystagmus," with a simultaneous adduction deficit of the fellow eye. The patients also displayed mild nystagmus in upgaze and downgaze. However, the authors observed that, unlike Millard-Gubler's and Weber's syndromes, there was no eye deviation in primary gaze. Convergence, eyelids, and pupils were also normal.

Sensormotor abnormalities contralateral to the side of the adduction weakness were present.6 Weakness of the limbs was mild, but voluntary motor function was grossly impaired, with a static tremor of "grand oscillation," athetoid movement of the fingers, ataxia, dysmetria, and difficulties of gait characteristic of cerebellar "asynergy." Sensory impairments sometimes involved the face, but dysesthesias of unrelenting cold, pin-prick, and pins and needles of the fingertip were uniform. There was impaired joint sensation in the hands and feet, "cutaneous hypoaesthesia of all modalities," and loss of stereognostic sense.

In each of the cases, the crossed paralysis was attributed to an enlarging bilateral solitary tubercule in the rostral tegmentum. The authors carefully plotted the initial midline location of the lesion in the rostral pons. The ocular findings of their patients (specifically, the absence of primary deviation) and histologic confirmation indicated to Raymond and Cestan that the third- and sixth-nerve nuclei were not impaired. They, therefore, called the position of the lesion "inter-nuclear," identifying (without naming) an internuclear ophthalmoplegia. The Salpêtrière neurologists contrasted their syndrome protubérantiel supérieur (superior pontine) to Weber's syndrome pédonculaire (peduncular) and Millard-Gubler's syndrome protubérantiel inférieur (inferior pontine).6

Directly comparing their findings with Grasset's review,8 Raymond and Cestan argued that paralysis of conjugate eye movements in their patients occurred without involving the sixth-nerve nucleus.6 The authors considered that the tubercule could have damaged the abducens nucleus from afar, via altered
vascularization or "tuberculous toxins." However, they reasoned that the absence of peripheral facial paralysis demonstrated the integrity of the facial colliculus and, hence, the sixth-nerve nucleus. In one of their patients an abduction deficit evolved, and histologic examination confirmed that the sixth-nerve fibers were directly damaged. Raymond and Cestan hypothesized that the deficit of horizontal eye movements (ie, internuclear ophthalmoplegia) in their patients was caused by a destruction of the ascending pathway from the sixth to the contralateral third-nerve nucleus (ie, the medial longitudinal fasciculus).6

CONCLUSIONS

The Table summarizes the original clinical findings, localization, and structures most likely involved in the Millard-Gubler, Foville, Weber, and Raymond-Cestan syndromes. Some of the other major eponymic entities named for French and Viennese neurologists2,3,10-14 are also listed. In contrast to the crossed paralyses of Millard-Gubler, Foville, Weber, and Raymond-Cestan, these other eponymic syndromes have held less importance in modern neurology but are often quoted. The syndromes of Gelle12 and Brissaud and Sicard,13 for example, are simply minor variations of Millard-Gubler's syndrome.

The discoveries of the crossed brain-stem syndromes and the related discussions they provoked served, in many instances, to advance neuroanatomic principles. The clinical findings, with or without pathologic substantiation, helped verify the localization of several of the cranial nerves and nuclei (ie, third, fifth, sixth, seventh, and eighth), and further the understanding of the medial longitudinal fasciculus, horizontal conjugate gaze, and innervation of facial musculature.

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REFERENCES


