

BRANCHIAL MYOCLONUS: THE EXPRESSION OF ARCHAIC RESPIRATORY GILL MOVEMENTS IN MAN?

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Abstract

The hypothesis that branchial or palatal myoclonus is the result of the release of neuronal mechanisms that normally suppress primitive respiratory gill movements is discussed in light of comparative neuroanatomy. Such an analysis has not been previously undertaken. The evidence supports the stated hypothesis. Testable predictions are presented.

Branchial myoclonus, frequently referred to as palatal myoclonus, is a central nervous system disorder that occurs in man. The disorder is manifested clinically by continuous, rapid, rhythmic, involuntary movements of the branchial derived muscles of the pharynx, larynx, neck, and face (Marsden, Hallett and Fahn, 1982). The frequency of these movements averages about 100-120/minute and ranges between 60 and 180/minute. Branchial myoclonus is unusual among movement disorders in that the abnormal movements persist through sleep (Marsden, Hallett and Fahn, 1982; Herrmann and Brown, 1967) and even through deep coma (Klien, 1918). It is caused by a variety of central nervous system destructive lesions but has a specific neuropathological findings. Because of its periodicity, persistence and its limited involvement to branchial muscles it has been suggested that branchial myoclonus results as a release phenomenon of primitive gill respiratory movements (Stern, 1949; Yakovlev, 1956; Lapresle, 1979). More generally, this implies that in the evolution of the central nervous system, primitive functions are not eliminated but suppressed or modified. This paper examines this hypothesis with the aid of comparative phylogenetic data.

History

Branchial myoclonus was first described by Politzer in 1862 (Guillain, 1938). Further and more refined descriptions followed by Schwartz in 1865, Boeck in 1866 (Guillain, 1938) and Spencer in 1886 (Stern, 1949). Good pathological and histological studies did not appear until the 1930s; and effective treatment became available in the 1970s (Magnussen, *et al.*, 1977; Williams, Goodenberger and Calne, 1978; Sakai, Shiraishi and Murakami, 1981; Gauthier, Young and Baxter, 1981). Several

hypotheses have been put forward to explain this very unusual movement disorder. These hypotheses have generally reflected the state of knowledge of the time. Thus, early hypotheses centered on anatomy (Guillain, 1938; Herrmann and Brown, 1967) while recent ones highlight neurophysiology (Matsuo and Ajax, 1979). The strong resemblance of branchial myoclonus to respiratory movements of fish, has been rediscovered by several generations of scientists (Stern, 1949; Yakovlev, 1956; Lapresle, 1979).

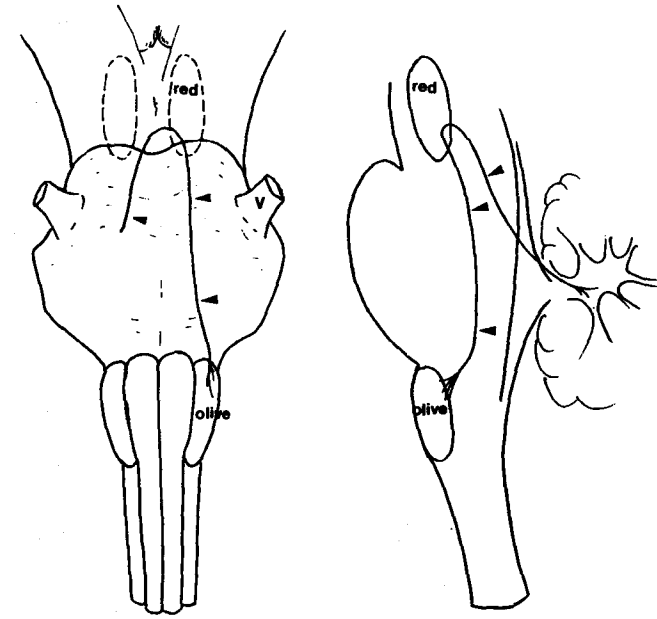
Pathological Features

The most notable pathological feature is hypertrophy of the inferior olivary nucleus in the medulla (Jellinger, 1973; Gautier and Blackwood, 1961). Microscopically the hypertrophy is the result of scarring and vacuolar degeneration (Gautier and Blackwood, 1961; Aberfeld, 1966). These pathological changes result as a consequence of the loss of afferent input to the olivary nuclei from fibers traveling within the central tegmental tract. This tract carries information from the dentate nucleus in the cerebellum and the red nucleus in the midbrain. Normally the inferior olivary nuclei process this information and return it to the cerebellum. It was this triangular arrangement (the so-called Guillain-Mollaret Triangle) that led to the erroneous hypothesis that a feedback loop between these three nuclei was responsible for inhibiting pacemaker cells in the medulla (Herrman and Brown, 1967). More careful study has revealed that destruction of a specific pathway, the dentato-olivary pathway (Figure 1), which runs without synapsing from the dentate nucleus to the contralateral inferior olivary complex of nuclei is specifically responsible for the production of branchial myoclonus (Lapresle, 1979). Damage to any of the associated structures (i.e., dentate nucleus or central tegmental tract) with sparing of the dentato-olivary pathway may produce olivary hypertrophy without branchial myoclonus (Jellinger, 1973).

Clinical Features

As previously stated, the most remarkable clinical feature of branchial myoclonus is its periodicity and persistence through sleep. Muscles of branchial origin are always involved, and muscles of the shoulders and trunk may also become involved in severe cases. Unusual rotary eye movements are frequently described (Tahmouh, Brooks and Keltner, 1972; Chokroverty and Barron, 1969; Culebras, 1978).

Stroke is the most common cause of branchial myoclonus but other destructive diseases such as multiple sclerosis, syphilis, encephalitis, head trauma, or masses of varying sources may also produce it. There is almost always a lag of several months between the causative lesion and the recognition of branchial myoclonus (Matsuo and Ajax, 1979). The appearance of branchial myoclonus is gradual so that initially the patient may not be aware of it. However, once established, branchial myoclonus remains unchanging and very rarely improves (Guillain, 1938; Jacobs, Newman and Bozian, 1981). Treatment is accomplished with serotonin precursors or serotonin



DENTATO-OLIVARY PATHWAY

Figure 1. The dentato-olivary pathway depicted schematically in the brainstem of man. Red = red nucleus; olive = olivary nuclei; V = trigeminal nerve root.

agonists (Magnussen, *et al.*, 1977; Williams, Goodenberger and Calne, 1978; Sakai, Shiraishi and Murakami, 1981; Gauthier, Young and Baxter, 1981), which only ameliorates the abnormal movements.

Embryology and Comparative Neuroanatomy

The mammalian olive includes three nuclei: the large and conspicuous dentiform chief olivary nucleus, and the smaller medial accessory and dorsal accessory nuclei. Phylogenetically, the medial accessory nucleus is the oldest, and a homologous structure exists in the petromyzonts (lampreys), elasmobranchs (e.g., sharks) and teleosts (bony fishes). In the marsupials and lower mammals the accessory nuclei (particularly the medial) predominate. The chief olivary nucleus becomes prominent only in

higher mammals and particularly primates. The development of the olivary nuclei, and particularly the chief olivary nucleus, parallel the development of the dentate nucleus which is, in turn, related to the expanding role of the muscles of the distal extremities (Sarnat and Netsky, 1974). Evolution of the entire rubro-dentato-olivary system is intimately related to elaboration of the movement of the extremities, and its major role appears to be modification of fine movements particularly of the distal extremities (Sarnat and Netsky, 1974). It is thus not surprising that this system is very poorly developed in fish.

In humans the major efferents of the Purkinje cells of the cerebellum run to the midline cerebellar nuclei, particularly the dentate; while major afferents to the olive are from the red and dentate nuclei. Fish lack both red and dentate nuclei. In fish the major efferent cerebellar projections are to reticular cells in the midbrain; likewise, olivary afferents are from these midbrain reticular cells. These reticular cells of the archaic midbrain give rise to both the dentate and red nuclei (Sarnat and Netsky, 1974).

As the number of gill slits decrease and eventually disappear through evolution derivations of the gill arches became incorporated into new functions unrelated to respiration, but they maintain their innervation by the original branchial nerves. In man, branchial-derived muscles are found through the face, throat, and neck. Specifically, muscles innervated by the maxillo-mandibular divisions of the trigeminal (V), facial muscles of the facial (VII) and laryngeal, pharyngeal, and palatal muscles of the glossopharyngeal (IX) and vagus (X) nerves are all derived from branchial arches that serve a respiratory function in teleosts.

Respiratory Control in Fish

The respiratory center in fish is located in dorsal caudal medulla. It is almost completely autonomous and will continue normal rhythmic respirations even after transection as low as the facial lobe (Hughes and Shelton, 1962). The actual number of involved neurons varies with the "depth of respiration" (Hughes and Shelton, 1962). The respiratory rate in most resting teleosts varies between 60 and 100 (Hughes and Shelton, 1958). In some fast moving fish the respiratory rate is modified by water speed. For example, in *Remora remora* gill movements are totally inhibited by water speeds of 60 cm/second (Muir and Buckley, 1967). Other fast swimming fish, like the tuna, have totally lost the ability to pump water through their gills (Brown and Muir, 1970). The neuronal mechanism that inhibits gill movements in these fish has not been delineated, but one should not necessarily expect it to be similar to that that has developed through evolution of air-breathing animals since the evolutionary pathways are different. Cerebellar activity has been variously reported to be inhibitory (Hughes and Shelton, 1962) or have no effect (Springer, 1928) on respiration of teleosts. Finally, oxygen tension also plays a role in respiratory movements. Although low oxygen partial pressures may actually reduce the respiratory rate of various fish (Lutz, 1930; Butler and Taylor, 1975) the activity of the respiratory muscles increases (Hughes and Ballantijn, 1968) suggesting an increase in the tidal flow. Further, it has been shown that general restlessness and activity (Jones, 1952) as well as fin and tail movements increase in low oxygen environments (Babak, 1911; Polimanti, 1912).

Relationship of Branchial Myoclonus to Respiratory Movements of Fish

The rhythmic movements of branchial derived muscles at a constant rate of 60 to 180/minute, superficially resembles the rhythmic movements of mouth and gill movements of fish which respire at a similar rate. The further involvement of shoulder and trunk muscles in severe cases of branchial myoclonus is analogous to the recruitment of fin and tail movements in oxygen deprived fish.

The persistence of branchial myoclonus through sleep and coma, and the general inability of the patient to wilfully modulate these movements strongly supports an autonomous group of rhythmically active cells similar to the medullary respiratory center of fish.

The specific involvement of the dentato-olivary pathway in the pathogenesis of branchial myoclonus implies that a specific system has evolved to inhibit aquatic respiratory movements in air breathing animals. The lack of a chief olivary nucleus in lower mammals suggests that the medial accessory nucleus is specifically involved in the suppression of rhythmic branchial movements.

The several months lag time between the destruction of the dentato-olivary tracts and the appearance of clinical branchial myoclonus suggests that the system of inhibition of branchial movements is multisynaptic. Finally, the response to serotonin suggests that the neurons involved in the inhibition of these movements normally receive serotonergic afferents.

Predictions

Predictions can be made which, if confirmed, would strongly support the above hypothesis.

Since in fish respiration the opening of the mouth precedes opercular opening by fraction of a second (Hughes and Shelton, 1958). The confirmation of a time difference between the myoclonus of trigeminal-innervated muscles and pharyngeal muscles would strongly strengthen the analogy. Electrical confirmation with electromyography is necessary since the time difference is too brief to be noted by clinical or slow-motion video examination (El-Mallakh, unpublished).

Since the trochlear nerve is probably of branchial origin (Sarnat and Netsky, 1974) it is suggested that the rotary eye movements frequently observed in branchial myoclonus (Tahmouh, Brooks and Keltner, 1972; Chokroverty and Barron, 1969; Culebras, 1978) are due to intortion caused by superior oblique myoclonus. Although a recent detailed analysis of three patients with asymmetric branchial myoclonus and intortion of one eye revealed extortion of the partner eye (Nakada and Kwee, 1986), a case of equally bilateral branchial myoclonus would be predicted to exhibit bilateral intortion.

Finally, since the chief olivary nucleus is a modern structure that evolved to control the distal extremities it probably is only incidentally involved in branchial myoclonus. Experimental documentation of typical branchial myoclonus following destruction of afferents to the medial accessory nucleus would essentially confirm the hypothesis.

Summary

The hypothesis has been previously forwarded that an uncommon human neurologic disease, branchial or palatal myoclonus, actually represents the unmasking of gill respiratory movements. A previous detailed analysis of this hypothesis has not been previously undertaken. The relevant clinical, pathological, and experimental data are reviewed and provide strong support for this hypothesis. This preservation of primitive neurological structures and functions is compatible with the view that the present structure and function of the central nervous system is reflective of its evolutionary history (Halstead, 1968; Springer, 1928).

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