Comparative Anatomy of the Cerebellum

If we can discover what functional factors were primitively concerned in the initial differentiation of the cerebellum from preexisting bulbar structures and some of the steps by which additional functional systems of diverse kinds were drawn into the cerebellar complex, some light may be shed on the great problems of the analysis of higher cerebellar functions.   (C. J. Herrick 1924b)

It is from the standpoint that a brief survey of the circumstances under which the cerebellum and its Purkinje cells developed in phylogeny could shed some light on the evolution of its organization and functions in higher forms that this review, mostly from classical sources, is presented. This survey is based primarily on the following sources: Ariëns Kappers, Huber, and Crosby (1960), Crosby (1969), Herrick (1924a, 1924b), Larsell (1967), Larsell and Jansen (1972), Llinás (1969), Llinás and Hillman (1969), Nieuwenhuys (1967), Schnitzlein and Faucette (1969), Butler and Hodos (1996), and Nieuwenhuys, ten Donkelaar, and Nicholson (1998). Some additional aspects of comparative anatomy of the cerebellum are included in Chapter 12, which discusses cerebellar-like structures in certain fish, including the valvula of mormyrid fish, the electrosensory lobe, and the mammalian dorsal cochlear nucleus.

2.1. Origins of the Cerebellum

Larsell (1967; pp. 6–7) summarized the early phylogeny of the cerebellum as follows:

The primitive predominantly vestibular and lateral-line organ cerebellum of the lampreys [eel-like fish with a round mouth] is continued in the sluggish urodeles [tailed amphibians] and higher forms as a laterally situated vestibular and lateral-line subdivision, medial to which develops a corpus cerebelli whose fiber tract connections are quite different. The corpus cerebelli receives proprioceptive and other sensory impulses and becomes the predominant feature of the cerebellum

in the vertebrates above the sluggish urodeles, as well as in the active types of fishes such as selachians [sharks, skates, and rays] and teleosts [bony fish].

Microscopically, it is evident that precursors of Purkinje cells arose amid granule cells, first irregularly in location and then in a progressively layered fashion: the layer of Purkinje cells. The Purkinje cells themselves progressively developed extensive dendritic trees that increasingly become confined to a single plane, through which the parallel fibers (the axons of granule cells) thread, initially in a somewhat random fashion but increasingly at right angles, not unlike the wires strung on the cross-arms of telephone poles of former times.

In a departure from the main trend of cerebellar evolution, the valvula (Chapter 12) develops in association with the lateral line organs and electrosensory system of certain fish, becoming large enough to cover the rest of the brain. In the detailed anatomy of this unusual structure, the molecular layer (constituted of the parallel fibers and apical dendritic tree of the Purkinje cells), as well as the layer of Purkinje cells themselves, becomes greatly folded or foliated. The granular layer of granule cells, however, does not participate in this folding, nor do its axons bifurcate; the parallel fibers arise directly from the granule cells. This arrangement must be of special significance in relation to the processing of data from lateral line organs and electroreceptors, perhaps in the capacity of phased arrays for beam forming (Chapter 12).

The origin of the cerebellum in close association with nuclei of the eighth (vestibular) nerve and the lateral line nerves perhaps suggests that this part of the cerebellum originated as a means of carrying out some type of transformation of the coordinate system of input data from the vestibular organ and the lateral line organs. Bullock (1969) suggested that the function of the cerebellum might be along the lines of an organ primarily computing and representing, in some analogue fashion, an image of the relations of the body in space. In this connection, it is relevant to note that, in the counterpart of the vestibular system among manmade navigation systems (i.e., the so-called strap-down or vehicle-oriented inertial navigation systems), such a transformation of coordinates must be carried out by a central computer on the basis of the input data from the motion sensors (angular, rectilinear; Barlow 1964, 1966; Siouris 1993; see also Chapter 12). It should be noted that this part of the cerebellum in lower forms, and its counterpart in higher forms (as the flocculonodular lobe), is slightly different in its histology from the main body of the cerebellum (corpus cerebelli). Thus, Brodal (1967) pointed out that the mossy fibers in the flocculus and nodulus (and also the caudal part of the uvula and the dorsal paraflocculus) of the cat, vestibular fibers terminate with more profuse branching and a greater number and density of terminal globules than is the case with the "classical" (nonvestibular) type of mossy fibers. A relatively greater number of Golgi cells appeared to be associated with these "vestibular" mossy fibers.

2.2. Fish

In vertebrates, the cerebellum develops from two bilaterally symmetrical formations located dorsally at the upper end of the medulla oblongata (the rhombencephalon),
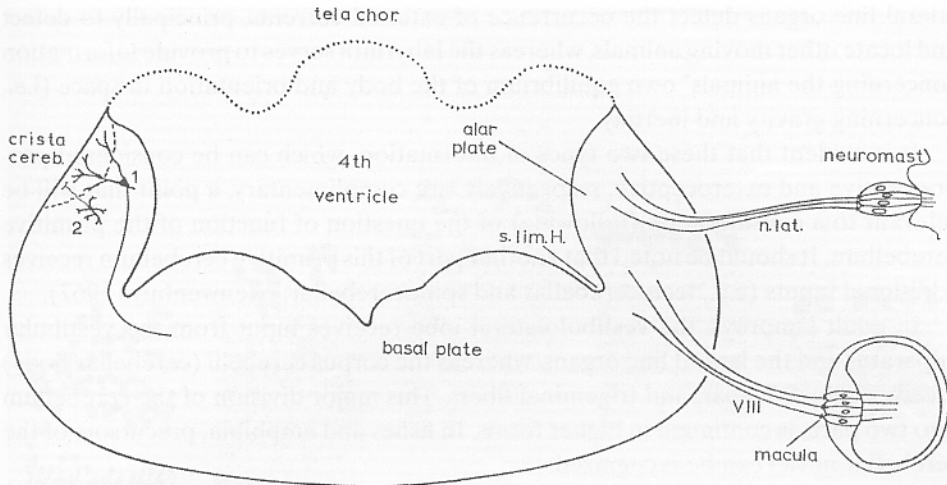
Figure 2.1. Diagrammatic transverse section through the upper medulla oblongata of a lamprey, showing (on the right) the similarities between receptor cells of the lateral line nerve and the vestibular nerve, and (on the left) the crista cerebellum or prototype cerebellum with a precursor Purkinje cell (1) and granule cell (2). crista cereb., crista cerebellaris; n. lat., nervus lateralis; tela chor., tela choroidea; s. lim. H., sulcus limitans of His. (From Nieuwenhuys 1967; reprinted by permission of the author.)

in the region of termination (in their respective nuclear complexes) of the fibers from the eighth or vestibular nerve and the lateral line nerves. This area is sometimes termed the area octavolateralis. Thus, the oldest afferent paths to the cerebellum are those of the vestibular and, in fish (and also in amphibia), of the lateral line systems. This area is also the area of termination of the trigeminal nerve. This arrangement is illustrated in Figure 2.1 for the lamprey (a member of the cyclostomes, that is, eel-like fish having a round suctorial mouth and having a brain length of 1 centimeter). The lamprey is the lowest form in which there is a clearly distinguishable cerebellum. Whether still lower forms of vertebrates possess a cerebellum (e.g., the myxinoids, the most primitive living vertebrates) has been an issue of much debate (Nieuwenhuys 1967).

In bony fish (teleosts), it has been proposed that the cerebellar auricles, which receive a large input from the vestibulolateral line system, constitute the vestibulo-cerebellum and are the homologues of the flocculonodular lobe of higher vertebrates, whereas the corpus cerebelli, receiving spinocerebellar and tectocerebellar fibers, is the homologue of the vermis of higher vertebrates (Ariëns et al. 1960).

It is relevant to note that the labyrinth (the three semicircular canals together with the saccule and utricle) and the lateral line organs of lampreys (*Petromyzontidae*) have a remarkable structural, as well as functional similarity, which is evident from the right side of Figure 2.1. An important difference between the two structures is that the arrangement of the lateral line organs is such that they are sensitive to relative motion of the fluid surrounding the animal, whereas the labyrinths, having basically the same sensing mechanism, are sensitive to fluid, the endolymph, which is trapped in the labyrinths. Thus, by means of detection of the motion of fluid, the

lateral line organs detect the occurrence of external currents, principally to detect and locate other moving animals, whereas the labyrinth serves to provide information concerning the animals' own equilibrium of the body and orientation in space (i.e., concerning gravity and inertia).

It is evident that these two types of information, which can be considered pro-prioceptive and exteroceptive, respectively, are complimentary, a point that will be relevant to a consideration (following) of the question of function of the primitive cerebellum. It should be noted that another part of this primitive cerebellum receives additional inputs (e.g., tectocerebellar and spinocerebellar; Nieuwenhuys 1967).

In adult lampreys, the vestibulolateral lobe receives input from the vestibular apparatus and the lateral line organs, whereas the corpus cerebelli (cerebellar body) receives spinal, bulbar, and trigeminal fibers. This major division of the cerebellum into two parts is continued in higher forms. In fishes and amphibia, precursors of the cerebellar nuclei can be recognized.

Histologically, the area of the brain of lampreys in which the two nerves (vestibular and lateral line) terminate consists principally of small granular cells that have a few short dendrites and a laterally directed axon that bifurcates longitudinally (Fig. 2.1, left side, 2). These bifurcated axons are the forerunners of the parallel fibers. Scattered among the granular cells are larger neurons having long dendrites extending in the same direction as the axons of the granule cells (Fig. 2.1, left side, 1), with axons that may curve downward and medially. These are the precursors of the Purkinje cells. The neuropil zone of intermixing of the axons of the granular cells and the dendrites of the larger cells is termed the crista cerebellaris or cerebellar crest, also known as the molecular layer. The two intermingled cell types form a cell layer. The small granule cells are equivalent to those in higher forms, and change little in phylogeny. The larger cells have been considered, as just mentioned, to be the precursors of Purkinje cells. It should be noted, however, that true Purkinje cells are characterized, among other features, by the fact that their dendrites branch in a single plane, whereas the dendritic tree of the larger cerebellar cellular elements is not confined to one plane (Nieuwenhuys 1967).

The cerebellum of cartilaginous fish (sharks and rays) is considerably larger than, and much further differentiated than, that of the round-mouth fish (cyclostomes), and the larger ones display grooves in the cerebellum, the number of which increases with the size of the body. It is also in this group of fishes that the Purkinje cells spread their dendrites, which are covered with numerous spines, in a single plane. Of particular note is the fact that the cartilagenous fishes have an olivocerebellar system, which accompanies the caudal portion of the spinocerebellar tract toward the body of the cerebellum (corpus cerebelli). The olivocerebellar fibers originate from the contralateral inferior olive and terminate in all parts of the body of the cerebellum.

2.3. Amphibia and Birds

In comparison with the salamander (Urodela, or tailed species), frogs (Anura, or tailless species) show a much more massive and more highly differentiated development of the cerebellum. This applies particularly to the Purkinje cells, which now
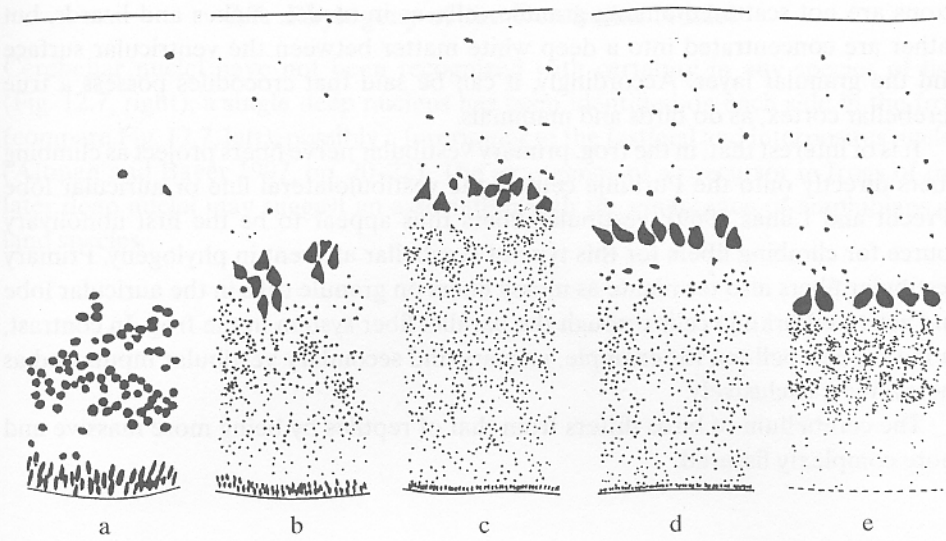
Figure 2.2. Sections showing the cell picture of the cerebellum of some representative vertebrates: (a) lamprey, (b) lungfish, (c) turtle, (d) lizard, and (e) pigeon. Note the progressive trend toward strict layering of the Purkinje cells from (b) to (e), and the diminution of size of granule cells after (a). (From Nieuwenhuys 1967; reprinted by permission of the author.)

constitute a distinct zone between the granular and the molecular layers (see Fig. 2.2 for the general trend toward layering). Further, the dendrites of the Purkinje cells are clearly oriented in a sagittal plane and show a more complex ramification (see Fig. 2.3 for the general trend). In crocodiles, the cerebellar cortical afferent and efferent
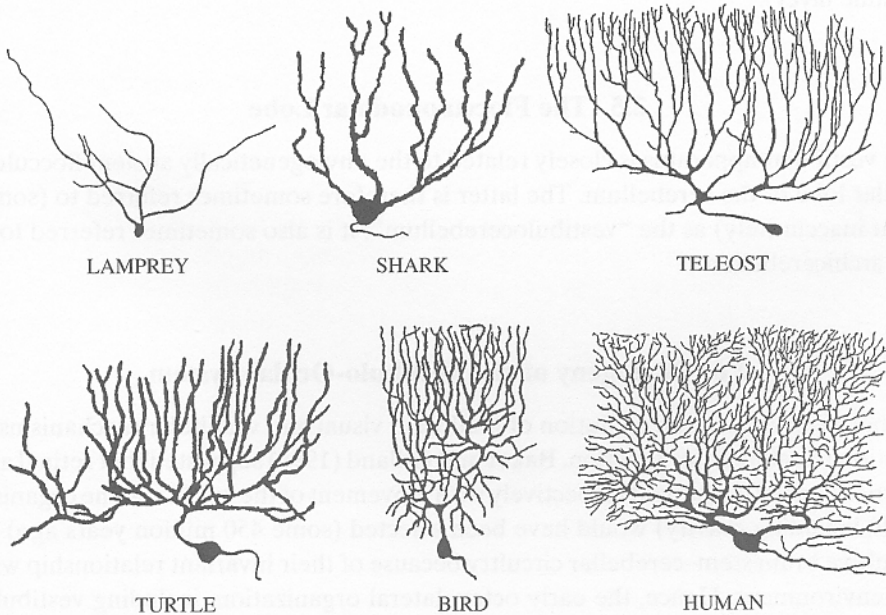

Figure 2.3. The progressive elaboration of Purkinje cell dendritic tree from lower vertebrates to humans. (From Nieuwenhuys 1967; reprinted by permission of the author.)

axons are not scattered among granule cells, as in turtles, snakes and lizards, but rather are concentrated into a deep white matter between the ventricular surface and the granular layer. Accordingly, it can be said that crocodiles possess a true cerebellar cortex, as do birds and mammals.

It is of interest that, in the frog, primary vestibular nerve fibers project as climbing fibers directly onto the Purkinje cells in the vestibulolateral line or auricular lobe (Precht and Llinás 1969); vestibular fibers thus appear to be the first nonolivary source for climbing fibers for this type of cerebellar afferent in phylogeny. Primary vestibular fibers also terminate as mossy fibers on granule cells in the auricular lobe and activate Purkinje cells through the parallel fiber system in the frog. In contrast, in the cat cerebellum, for example, primary and secondary vestibular inputs end as mossy fibers exclusively.

The cerebellum of birds differs from that of reptiles by being more massive and more complexly fissured.

2.4. Afferent Fiber Systems to the Cerebellar Cortex

Llinás and Hillman (1969) suggested that, whereas the climbing fiber system appears to represent a very primitive input to the cerebellar cortex, which has not changed very much in phylogeny, the mossy fiber granule cell system has undergone large changes. Among these changes is the large development of the molecular layer in higher vertebrates and the enormous increase in the number of synapses between parallel fibers and Purkinje cells as well as the development of inhibitory cells in the molecular layer (i.e., the stellate and basket cells, as well as the Golgi cells of the granule layer).

2.5. The Flocculonodular Lobe

The vestibular apparatus is closely related to the phylogenetically ancient flocculon-odular lobe of the cerebellum. The latter is therefore sometimes referred to (some-what inaccurately) as the "vestibulocerebellum"; it is also sometimes referred to as the archicerebellum.

2.6. Phylogeny of the Vestibulo-Ocular System

In their overview of the evolution of hindbrain visual and vestibular mechanisms in relation to oculomotor function, Baker and Gilland (1996) suggested that retinal and inertial signals (concerned respectively with movement of the world and the organism itself, including gravity) would have been selected (some 450 million years ago) by primitive brain stem–cerebellar circuitry because of their invariant relationship with the environment. Hence, the early octavolateral organization, including vestibular nuclei, would lead to an integrated inertial and visual coordinate system.

2.7. Phylogeny of the Cerebellar Nuclei

Cerebellar nuclei have not been recognized with certainty in any species of fish (Fig. 12.7, right); a single deep nucleus has been identified on each side in the frog (compare Fig. 12.7, left), possibly a forerunner of the fastigial and interpositus nuclei (Altman and Bayer 1997, pp. 20–22). The emergence of a precursor in frogs of the later deep nuclei may suggest an association with the emergence of amphibians as land species.