Chapter 23
Basket Cells

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Abstract Santiago Ramón y Cajal provided a definitive description of the basket cells of the cerebellum. Ramón y Cajal discovered a characteristic terminal plexus of basket cells around Purkinje cell somata, naming this the pericellular nest or nid. This was the first clear observation of an axon terminal in the central nervous system; the discovery cultivated his ideas that nerve cells need only be in contact, not in continuity, with one another to transmit nerve impulse, and that the flow of the impulse is directed from the axon of one cell to the cell body of another. These ideas later came to fruition as his Neuron Doctrine (Palay S, Chan-Palay V Cerebellar cortex cytology and organization. Springer, Berlin, 1974).

Keywords Basket cell • Purkinje cell • interneuron

23.1 General

Basket and stellate cells are often collectively called molecular layer interneurons. Both are GABAergic interneurons that cast feed-forward inhibition to Purkinje cells, share similar developmental, molecular, and firing profiles, and are thought to represent a gradually varying cellular continuum (Zhang and Goldman 1996; Sultan and Bower 1998; Schilling et al. 2008). Nevertheless, basket and stellate cells have been distinguished neuroanatomically (Ramón y Cajal 1911; Palay and Chan-Palay 1974). Basket cells are situated in the basal one-third of the molecular layer, and target the soma and axon initial segment of Purkinje cells. In comparison, stellate cells reside in the superficial two-thirds of the molecular layer, and target Purkinje cell dendrites. Reflecting their distinct geometrical targeting, the two interneuron types are predicted to have different postsynaptic effects on Purkinje cells (Bower 2010). The basket-type somatic inhibition powerfully and rapidly influences on Purkinje cell spiking output, while the stellate-type dendritic inhibition

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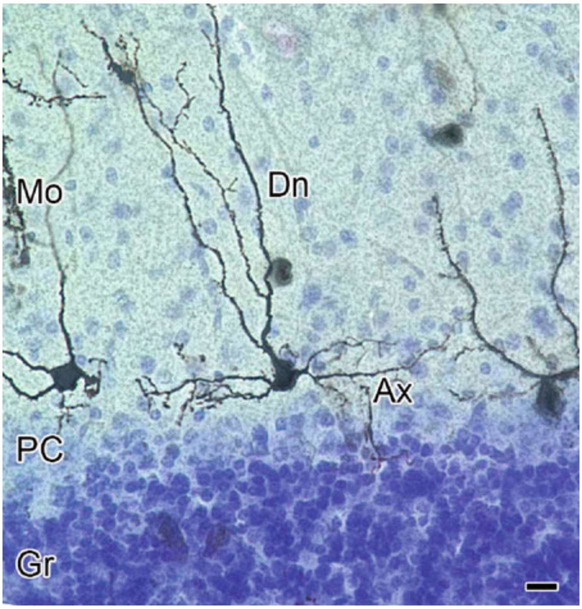

Fig. 23.1 Golgi staining of cerebellar basket cells in adult mice. Basket cells are situated in a basal one-third of the molecular layer, and extend moderately straight dendrites (*Dn*) in the parasagittal plane (this plane). Basket cell axons (*Ax*) originate from the soma or from one the major dendrites of basket cells. *Gr* granular layer, *Mo* molecular layer, *PC* Purkinje cell layer

counterbalances the parallel fiber excitation in local regions of Purkinje cell dendrites with no direct influence on Purkinje cell spiking output.

23.2 Cytology

The dendrites of basket cells are arborized in the parasagittal plane, and thus they are parallel to those of Purkinje cells and at right angles to the direction of parallel fibers (Fig. 23.1). The axons of basket cells also traverse in the parasagittal plane; they extend horizontally above Purkinje cell somata, and give off descending axon collaterals. Axon collaterals originating from three to seven basket cells form GABAergic perisomatic synapses on individual Purkinje cells, and further embrace the Purkinje cell axon initial segment by constructing the pinceau formation: an inverted cone-shaped structure beneath Purkinje cell somata (Sotelo and Llinas 1972).

23.3 Inputs

The soma and dendrites of basket cells receive excitatory inputs from parallel fibers, the bifurcated axons of granule cells. Parallel fiber-basket cell synapses are asymmetrical synapses formed mostly on dendritic shafts and occasionally dendritic spines (Palay and Chan-Palay 1974). Parallel fiber-basket cell synapses show a unique form of synaptic plasticity. Activation of extrasynaptic NMDA receptors on interneurons induces long-term synaptic plasticity by changing postsynaptic AMPA receptors from GluA2-lacking (Ca^{2+}-permeable) to GluA2-containing (Ca^{2+}-impermeable) receptors (Liu and Cull-Candy 2000). Parallel fiber-basket cell synapses also express the delta-type glutamate receptor GluD1, which strengthens the connectivity of this synapse (Konno et al. 2014). Basket cells also receive inhibitory inputs from basket and stellate cells and recurrent Purkinje cell axons.

Although several studies reported the presence of climbing fiber-interneuron synapses in the molecular layer, their contact lacks any kind of conventional synaptic specialization (Hámori and Szntágothai 1980; Kollo et al. 2006). When stimulating climbing fibers, no excitatory postsynaptic currents are elicited in molecular layer interneurons, but interneurons are activated via glutamate spillover from nearby climbing fibers (Szapiro and Barbour 2007). In turn, molecular layer interneurons send climbing fiber-driven feed-forward inhibition to Purkinje cells to prolong the post-complex spike pause (Mathews et al. 2012).

23.4 Outputs

Basket cells form a number of symmetrical synapses on the soma and axon hillock of Purkinje cells, but such synapses are rare along the axon initial segment of Purkinje cells (Palay et al. 1968; Somogyi and Hamori 1976; Iwakura et al. 2012). GABAergic molecules, including glutamic acid decarboxylase for GABA synthesis, vesicular inhibitory amino acid transporter for GABA filling into synaptic vesicles, and plasmalemmal GABA transporter GAT-1 for re-uptake of GABA, are highly concentrated in basket cell terminals synapsing on Purkinje cell somata, but are loosely organized in the pinceau formation (Iwakura et al. 2012). Likewise, $GABA_A$ receptor α1 and neuroligin-2, a synaptic adhesion molecule selective at inhibitory synapses, are highly accumulated on the postsynaptic membrane of perisomatic basket cell synapses, but virtually lacking in the axon initial segment (Iwakura et al. 2012). This distinct organization strongly suggests that the major target of GABAergic inhibition by basket cell outputs is the soma of Purkinje cells.

From around birth, climbing fibers constitute a dense plexus around Purkinje cell somata called the pericellular nest, and innervate perisomatic spine-like protrusions or thorns (Ramón y Cajal 1911; Larramendi 1969). By the end of the second postnatal week of rodent's life, mono-innervation by single climbing fibers is established in most Purkinje cells by dendritic translocation of single 'winner' climbing fibers and subsequent elimination of perisomatic climbing fiber synapses (Hashimoto et al. 2009). Almost simultaneously, axon collaterals of basket cells descend to form inhibitory pericellular synapses (Larramendi and Victor 1967), and further construct the pinceau formation in the third postnatal week (Ango et al. 2004). A subcellular gradient of the cell adhesion molecule neurofascin, which is formed along the axon initial segment-soma axis of Purkinje cells with the aid of Ankyrin-G, guides basket cell axon collaterals to the specific sites (Ango et al. 2004).

During the reorganization of perisomatic synapses, a considerable fraction of somatic spines innervated initially by climbing fibers are succeeded by basket cell axons and Bergmann glia, and the switching of postsynaptic receptor phenotypes from glutamatergic to GABAergic proceeds under the coverage of basket cell axons (Ichikawa et al. 2011). The establishment of perisomatic basket cell synapses influences climbing fiber-induced Ca^{2+} transients in the soma of Purkinje cells, and regulates the elimination of surplus climbing fiber synapses from Purkinje cell somata (Nakayama et al. 2012).

23.5 Pinceau Formation

The pinceau formation is composed of finger-like processes of basket cell axons and astrocytes. Given the strategic location and similarity to the axon cap of teleost Mauthner cells, the pinceau formation is thought to control the ultimate output of Purkinje cells, through either GABAergic inhibition, electrical inhibition by imposing a passive hyperpolarizing potential on the axon initial segment (Korn and Axelrad 1980), or both. Unique features of the pinceau formation have been taken to support the hypothesis of electrical inhibition. The lack of Na^+ channels (Laube et al. 1996) and dense localization of *Shaker*-type K^+ channels $K_V1.1$ and $K_V1.2$, together with their scaffolding protein PSD-95 (Laube et al. 1996), may prevent active impulse conduction in the pinceau formation. Similarly, septate-like junctions between finger-like processes of basket cells, which should provide the pinceau formation with high resistance (Sotelo and Llinas 1972; Faber and Korn 1989), may allow currents to preferentially channel into the axon initial segment, thus leading to passive hyperpolarization. A recent electrophysiological study has shown that the pinceau formation exerts ultra-rapid axon-axon ephaptic inhibition of Purkinje cells (Blot and Barbour 2014).

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