



Purkinje Neurons: Development, Morphology, and Function

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Abstract

Cerebellar Purkinje neurons are arguably some of the most conspicuous neurons in the vertebrate central nervous system. They have characteristic planar fan-shaped dendrites which branch extensively and fill spaces almost completely with little overlap. This dendritic morphology is well suited to receiving a single or a few excitatory synaptic inputs from each of more than 100,000 parallel fibers which run orthogonally to Purkinje cell dendritic trees. In contrast, another type of excitatory input to a Purkinje neuron is provided by a single climbing fiber, which forms some hundreds to thousands of synapses with a Purkinje neuron. This striking contrast between the two types of synaptic inputs to a Purkinje neuron has attracted many neuroscientists. It is also to be noted that Purkinje neurons are the sole neurons sending outputs from the cerebellar cortex. In other words, all computational results within the cortex are transmitted by Purkinje cell axons, which inhibit neurons in the cerebellar or vestibular nucleus. Notably, Purkinje neurons show several forms of synaptic plasticity. Among them, long-term depression (LTD) at parallel fiber synapses has been regarded as a putatively essential mechanism for cerebellum-dependent learning. In this special issue on Purkinje neurons, you will find informative reviews and original papers on the development, characteristics and functions of Purkinje neurons, or related themes contributed by outstanding researchers.

Keywords Purkinje neuron · Dendrite arborization · Climbing fiber · Synapse formation · Synapse elimination · Synaptic plasticity · Motor control · Disease

Fujishima, Galbraith, and Kengaku review accumulating information about the processes of formation of characteristic Purkinje cell dendritic trees [1]. The space-filling and non-overlapping dendritic pattern of a Purkinje neuron is focused on in particular, and the contribution of contact-dependent avoidance to the formation of characteristic dendritic pattern is explained. They also discuss molecules involved in the dendrite formation such as neurotrophins, protocadherin, Slit, and Robo.

Nozawa et al. report a new method to study the subcellular localization of synaptic-adhesion molecules using Purkinje neurons [2]. The author group has been studying critical molecules involved in specific synapse formation on a Purkinje neuron and identified the GluD2, Cbln1, and Neurexin interaction in parallel fiber-Purkinje cell synapse formation. Here,

they report that epitope-tagging by gene editing with CRISPR/Cas9 is a powerful method for mapping endogenous synaptic organizer molecules with subcellular resolution.

Kano et al. review the process of elimination of surplus climbing fiber inputs to a Purkinje neuron during cerebellar development and its molecular regulation mechanisms [3]. The early and late phases of the elimination process are explained, and the roles of many molecules involved in the former, such as P/Q type Ca²⁺ channels, IGF-1, Semaphorin 3A, Plexin A4, Progranin-Sort 1, and C1q11-Bai2, and those involved in the latter, such as mGluR1, Gαq, PLCβ4, PKCγ, Semaphorin 7A, plexin C1, BDNF, TrkB, and Arc, are discussed.

Streng, Popa, and Ebner review various ideas about functional roles of climbing fibers and propose a new idea [4]. A climbing fiber exerts a powerful excitatory action on a Purkinje neuron resulting in generation of a complex spike, which influences the Purkinje neuron activity on short and long time scales. Various previous ideas about the function of climbing fibers such as event detection, error, rhythmicity and timing, gain change, and bistability hypotheses have been explained. The authors discuss each of them and then propose

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new dynamic encoding hypothesis stating that climbing fiber discharge controls signals encoded in the simple spike firing of a Purkinje neuron.

Suvrathan and Raymond thoroughly review induction protocols of LTD at parallel fiber to Purkinje neuron synapses, and they discuss how conflicting results on LTD have been reported [5]. Their recent interesting finding that the LTD induction condition varies across different regions of the cerebellum is also explained. The optimal interval between stimulation of parallel fibers and that of a climbing fiber differs and seems to fit for a particular motor learning paradigm.

I myself review induction conditions, modulations, interactions, and saturation of synaptic plasticity in a Purkinje neuron and discuss how multiple types of synaptic plasticity such as LTD, long-term potentiation at parallel fiber synapses, and rebound potentiation at inhibitory interneuron to a Purkinje neuron synapses might work together in motor learning paradigms [6].

Owens et al. address involvement of the cerebellum in a complicated task including perception, decision-making, and action in humans [7]. They examine pupillary response, eye movement, hand response, brain activity etc. during trajectory prediction and go/no-go tasks in expert baseball players and control non-experts. They report widespread involvement of the medial and lateral cerebellum together with the cerebral cortex in the task. They also show faster increase of pupillary size and less time of tracking in experts.

Van Dun, Mitoma, and Manto review therapeutic effects of non-invasive stimulation of the human cerebellum in various neurological and psychiatric diseases [8]. Effects of transcranial current stimulation or transcranial magnetic stimulation on cerebellar ataxias, essential tremor, dystonia, Parkinson's

disease, schizophrenia, bipolar disorder, major depressive disorder, generalized anxiety disorder, and obsessive disorder are concisely explained.

Compliance with Ethical Standards

Conflict of Interest The author declares that he has no conflict of interest.

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