PERSPECTIVES

Input–output plasticity of peripheral responses in cerebellar Golgi cells *in vivo*

Henrik Jörntell
Section for Neurophysiology and NeuroNano Research Center, BMC F10, Tornavägen 10, SE-221 84 Lund, Sweden

Email: henrik.jorntell@med.lu.se

In this issue of *The Journal of Physiology*, Xu & Edgley (2008) report on the induction of plastic changes in the response to peripheral stimulation in one of the major cerebellar cortical neurons, the Golgi cell. The response plasticity is induced by peripheral stimulation in combination with climbing fibre activation, but not by the same peripheral stimulation alone. Hence, this is a new form of climbing fibre-dependent cerebellar plasticity, which adds to the previously described long-term depression of parallel fibre input to Purkinje cells (Ito, 2006) and long-term potentiation of parallel fibre input to molecular layer interneurons (Jorntell & Ekerot, 2003; Rancillac & Crepel, 2004; Ito, 2006).

Papers from this lab have earlier reported on a peculiar peripheral response in Golgi cells located in crus I/II of the rat (Holtzman *et al.* 2006*b*). This response is a relatively long-lasting depression of spike activity which seems to be evoked from the skin of all four limbs as well as the snout. In addition, muscle afferents in the group II/group III range also activate this response, which is transmitted via the anterolateral system bilaterally (Holtzman *et al.* 2006*a*). It is very different from the more straightforward excitatory responses (presumed to be mossy fibre–Golgi cell and/or mossy fibre–granule cell–Golgi cell responses) that have been described for Golgi cells by other authors (Vos *et al.* 1999; Jorntell & Ekerot, 2006). Nevertheless, this is a very consistent phenomenon, which in the hands of this lab in principle works as a diagnostic criterion for a Golgi cell recording.

Interestingly, in this paper (Xu & Edgley, 2008) the authors show that a similar inhibitory response in Golgi cells can be evoked also after climbing fibre activation. However, this inhibitory response is not mediated by the same pathway as the peripherally induced inhibitory response since the peripheral stimulation evoked no climbing fibre responses in the local Purkinje cells. The inhibitory responses could be evoked by other cerebellar inhibitory neurons which are activated by climbing fibres and/or peripheral inputs, i.e. basket cells/stellate cells (Jorntell & Ekerot, 2003; Szapiro & Barbour, 2007), Purkinje cells and Lugaro cells (Dumoulin *et al.* 2001). Alternatively, inhibitory responses could be induced via special types of extrasynaptic receptors on Golgi cells, which would be activated by spill-over of glutamate from climbing fibres and/or peripheral afferent pathways.

However, the major new finding of this paper is that after conjunctive peripheral and climbing fibre activation for 20 min, the inhibitory responses evoked from the periphery are persistently reduced. Naturally, this could be explained by a long-lasting depression of the efficacy at the inhibitory synapse(s) on the Golgi cell. Alternatively, the depression could be the result of a reduced excitatory synaptic input to the presynaptic inhibitory cell. A third possibility would be changes to the efficacy of the extrasynaptic receptors. To provide a better clue about the locus/loci of plasticity, these experiments should ideally be repeated whilst recording from the other types of neurons.

This finding adds to recent literature that the cerebellum is highly prone to plastic changes *in vivo*. Of course, the functional consequences of this form of plasticity depend on the function of the Golgi cells. Recent *in vivo* recordings from their main postsynaptic targets, the granule cells, indicated that fast inhibitory responses are virtually lacking in the adult, non-anaesthetized animal, suggesting that the inhibitory granule cell control from Golgi cells may be primarily exerted on a long time scale (Jorntell & Ekerot, 2006), possibly related to overall context switching. This function seem to be in agreement with findings from a recent series of experiments from this laboratory, which shows us that Golgi cells are highly sensitive to inputs from a system that is traditionally viewed as being involved in arousal (Holtzman *et al.* 2006*a*). This system induces relatively long-lasting changes in Golgi cell excitability, the magnitude of which can be changed via climbing fibre-dependent plasticity (Xu & Edgley, 2008).

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