Anatomical structure alone cannot predict function

BEHAVIORAL AND BRAIN SCIENCES
20:2: 252-253, 1997

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Abstract

The central hypothesis of the target article that tidal waves of parallel fiber excitation precisely activate Purkinje cell spiking is hard to reconcile with recent neurophysiological and modeling data. The assumed pattern of mossy fiber input seems unrealistic, inhibition is likely to interfere with the proposed excitatory responses, and moreover, computer simulations show that the Purkinjecell is a poor coincidence detector.

While providing an interesting framework for understanding cerebellar function, the theory proposed by Braitenberg and colleaguesis limited mostly to neuroanatomical speculation. In this comment we will show that recent physiological and modeling data cast doubt on three essential components of the theory: the pattern of mossy fiber input, the purely lateral inhibition and the sensitivity of Purkinje cells to waves of parallel fiber input. Unless major enhancements to the theory are made, and direct experimental evidence *in vivo* is found, we find it unlikely that the cerebellum is operating according to the principle of parallel fiber tidal waves.

The authors propose that only those spatiotemporal patterns of mossy fiber input that evoke waves of parallel fiber activity are effective in stimulating Purkinje cells. The simplicity of this system may seem attractive, but if it is true most patterns of mossy fiber input would not change cerebellar output at all. Even if the fractured somatotopic maps of the granule cell layer (Shambes *et al*. 1978) were set up to generate such waves, one would be able to code at most a few input-output sequences for each beam. Moreover, it has been shown that these fractured somatotopic maps show very little plasticity (Gonzalez *et al*. 1993), which means that an animal would be born with a limited fixed repertoire of effective input sequences. This seems a rather inefficient way to control the complex adaptive dynamics of the motor system.

A second component of the theory is the purely excitatory response along the hypothetical narrow parallel fiber beam. The authors specifically dismiss the presence of inhibitory responses of Purkinje cells within this beam. Instead, inhibition is suggested to suppress activation of Purkinje cells

lateral to the beam. We believe that available experimental data contradict this hypothesis. Anatomically, stellate cell axons connect to Purkinje cells in the immediate vicinity of parallel fibers activating these cells (Sultan *et al*. 1995), which does not indicate a spared region of pure excitation. Even early recordings looking for beams of activated Purkinje cells with direct electrical parallel fiber stimulation in primates (Bloedel *et al*. 1972), found predominantly inhibitory responses along the center of the activated parallel fiber beam. A similar finding was made in the anesthetized rat, when parallel fibers were activated with sensory stimulation (Bower & Woolston 1983). The final component of the theory is the "decoder", i.e. the Purkinje cell which is supposed to act as a coincidence detector responding mostly to waves of parallel fiber activity. The authors' own experimental data, however, show that the Purkinje cell seems to be a poor decoder of wave-like parallel fiber activity. Their figure 10B shows that for identical "ideal" inputs the latency of the Purkinje cell response varied by 7 ms and had a 20% failure rate. In fact, input movement in the "wrong" direction sometimes caused responses with similar latencies to 40% of the stimuli (Fig. 10C). With responses already so variable in the slice preparation where Purkinje cells are mostly silent, one wonders how these cells firing at rates of 40 Hz and higher *in vivo* could reliably signal the presence of a wave during actual motor behavior. These experimental results match our modeling studies which suggest that even *in vivo* Purkinje cells can be quite sensitive to fast changes in the rate of parallel fiber input, but with a large jitter of the response (De Schutter 1994) and with little sensitivity to actual coincidence of the input (unpublished results). In our view it is unlikely that the Purkinje cell is a coincidence detector, instead it performs a complex integration over time of excitatory and inhibitory input (Jaeger *et al*. 1996).

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