Nature Reviews Neuroscience | Published online 6 Apr 2017; doi:10.1038/nrn.2017.47

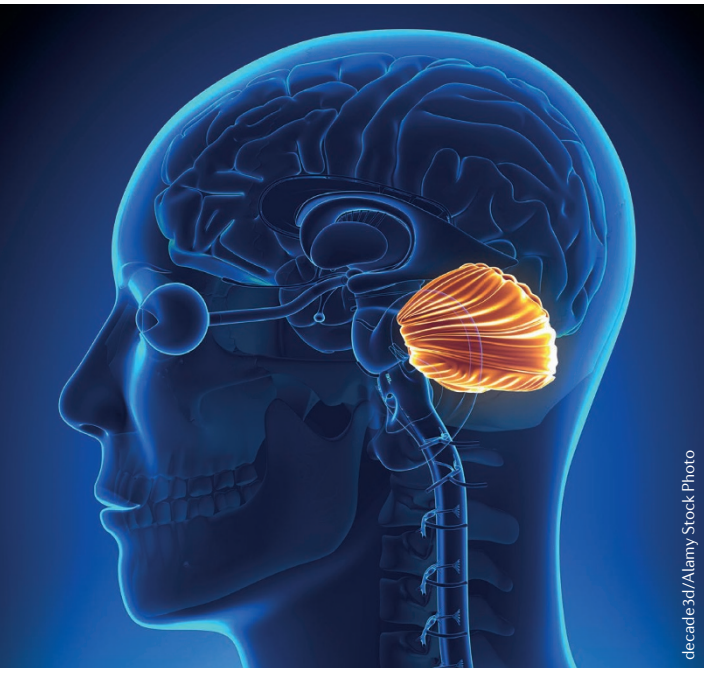
CEREBELLUM

The little learning brain

> many granule cells showed reward-related responses

Cerebellar granule cells receive inputs to the cerebellum and provide Purkinje cells with sensorimotor contextual information. Two recent studies used calcium imaging to investigate changes in granule cell activity during two different types of learning, providing insights into the function of these cells.

Giovannucci *et al.* measured calcium responses in granule cells in the cerebellar lobule VI in head-fixed mice over the course of classical eyeblink conditioning. In each trial, an aversive periorbital airpuff (the unconditioned stimulus (US)) was delivered to mice shortly after a flash of light or a mild puff of air was targeted to the ipsilateral whisker area (the conditioned stimulus (CS)). With repeated trials over several days, the mice learned to blink (a conditioned response (CR)) in anticipation of the airpuff.



decade3d/Alamy Stock Photo

Trial-by-trial analyses revealed that most granule cells responded to the US and the CS, and the activity of many of the granule cells was associated with different movements (for example, snout movement or locomotion), which was consistent with previous research indicating that these cells represent sensorimotor information. Importantly, almost two-thirds of the studied granule cells produced CR-related calcium responses; that is, responses that followed the CS and preceded the CR and that, in trials in which mice produced a CR (but not in trials in which they did not produce a CR), grew in amplitude with training. Thus, learning was accompanied by a widespread and dense granule cell response.

In the other study, Wagner *et al.* recorded calcium responses in granule cells in cerebellar lobules V and VI in head-fixed mice performing an operant task in which they moved a manipulandum with their forelimb to obtain a delayed sugar water reward. Again, many granule cells showed activity during different movements, such as forelimb movement or licking. Strikingly, many granule cells showed reward-related responses. Specifically, some granule cells showed activity during reward anticipation, whereas others preferentially responded during reward consumption (but not during licking when the reward was omitted). Furthermore, many neurons were sensitive to reward omission: some were active in anticipation of reward but became even more active if the reward was omitted, and others showed an increase in calcium signal only after the omitted reward. Granule cells in mice that were reconditioned to associate a tone with a normal or large sugar water reward showed similar reward-related signals; moreover, some of the other granule cells in these mice represented reward expectation or reward magnitude. These findings suggest that cerebellar granule cells represent different types of reward-related information.

The authors next investigated how granule cell responses changed with training on the operant task. Over the course of several days of training, fewer neurons responded to the reward, whereas more neurons became responsive to reward anticipation. In addition, the responses of granule cells that were most tuned to reward omission or reward anticipation at day 6 of training had become progressively stronger with each day of training, whereas granule cells that showed strong responses during forelimb movement showed little change in their responses with training. Therefore, reward-related granule cell responses are particularly dynamic during learning.

Together, these two studies describe changes in granule cell activity that occur with different types of learning, and imply that granule cells may provide much more than sensorimotor contextual information to Purkinje cells. Moreover, these studies provide support for the hypothesis that the cerebellum may be involved in various cognitive processes.

Natasha Bray

ORIGINAL ARTICLES Giovannucci, A. *et al.* Cerebellar granule cells acquire a widespread predictive feedback signal during motor learning. *Nat. Neurosci.* http://dx.doi.org/10.1038/nn.4531 (2017) | Wagner, M. J. *et al.* Cerebellar granule cells encode the expectation of reward. *Nature* http://dx.doi.org/10.1038/nature21726 (2017)