The cerebellum is involved in the main circuits that regulate social behavior in mice.

NEUROSCIENCE

The cerebellum gets social

The cerebellum can regulate behavior by controlling dopamine release

By **Egidio D'Angelo**

The cerebellum contains the second main cortex of the brain and ~50% of the neurons that constitute the brain. Although the cerebellum has long been thought to subserve motor learning and coordination, more recently it has been recognized to take part in cognitive and emotional processing. Additionally, evidence for cerebellar involvement in autism spectrum disorder (ASD), schizophrenia, and addiction is growing. On page 248 of this issue, Carta *et al.* (*1*) extend this theme and show that the cerebellum can activate the ventral tegmental area (VTA). The VTA is a mesencephalic nucleus giving rise to the mesocortical and mesolimbic fiber bundles that release dopamine to the prefrontal cortex and ventral striatum. Dopamine, in turn, plays a fundamental role in cognitive and emotional functioning by regulating motivation and reward. This places the cerebellum into the main circuits regulating brain states and social behavior.

Behavior can be defined as a coordinated series of motor acts and neurovegetative changes centered on a certain target (*2*). There are several elements that contribute to the behavioral response, and historically these have been separated and attributed to different parts of the brain. The cerebral cortex is classically thought to play a planning and decisional role; the basal ganglia to control action selection, motivation, and reward; the cerebellum to coordinate motor actions; and the hippocampus to allow spatial navigation (*3*). Although these stereotypes may help to conceptualize how the behavioral response is generated, they are oversimplifications (*4*) because brain circuits are interconnected at multiple levels and influence each other through neuromodulatory systems, as demonstrated by Carta *et al.*

The cerebral cortex is bidirectionally connected with the cerebellum through multiple neural circuits (*5*–*8*). In humans, these circuits involve the motor cortical areas but also areas that regulate cognition, emotion, attention, and social behavior. These nonmotor areas receive more than 80% of all the nerve fiber tracts that travel between the cerebellum and cerebral cortex through the deep cerebellar nuclei and thalamus (*9*).

The prototypical mode of action of the cerebellum has been characterized for motor coordination (*5*). The cerebral cortex elaborates the motor plan as a predictive sensory state (*6*, *7*), which is conveyed to the cerebellum through descending pathways. In the cerebellum this plan is compared to the actual sensory state, which is conveyed through the afferent sensory pathways. According to the motor learning theory, through this comparison the cerebellar circuit learns to minimize motor errors (*10*). It has been argued that this process could be generalized to the cognitive and emotional domains (*11*). The results of Carta *et al.* imply that a similar mechanism could be used to regulate the motivation and reward cycle.

In functional magnetic resonance imaging (fMRI) studies, different areas of the cerebellum are activated depending on the nature of tasks performed by the subjects. The anterior cerebellum is activated in relation to motor commands, whereas the posterior cerebellum and the hemispheres become activated when, for example, we see actions performed by others, we evaluate sensory perceptions, and we feel emotions (*12*). Moreover, the cerebellum shows coherent activation together with several areas of the cerebral cortex and hippocampus in the so-called fMRI resting-state networks. These include the default-mode network, the salience network, and the attention networks, which regulate the switch from an internal reference state to external target-oriented behaviors (*13*). The study of Carta *et al.* implies that the specific modules of the cerebellum, as part of these brain networks, contribute to action selection and behavioral switching.

Surprisingly, Carta *et al.* find that the cerebellum regulates the motivation and reward process that is typically attributed to the basal ganglia. The authors demonstrate that in mice, monosynaptic connections from the fastigial nucleus of the cerebellum regulate the activity of the VTA directly. In this way, the cerebellum can regulate functions related to decision-making, emotional control, and attentional switching. The same group showed that the cerebellum communicates directly with the basal ganglia (*14*). The findings of Carta *et al.* reveal a more complex scenario in which the two main subcortical circuits coordinate dopamine functions in the brain.

Carta *et al.* suggest that dysfunction of the cerebellum-VTA connection could contribute to the pathogenesis of diseases in which the dopaminergic system is dysregulated, including ASD and schizophrenia (*15*), and to conditions such as drug addiction. These proposals need critical validation in humans. This study opens a new avenue for interpreting the function of the cerebellum and also for understanding social behavior and related pathologies, with the potential to discover novel therapies to treat these diseases. ■

Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy. Email: dangelo@unipv.it

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