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Many studies of motor learning have focused on synaptic plasticity in the cerebellar cortex. There is evidence that nuclei targeted by the cerebellar cortex also contribute to memory storage, but the lack of a molecular understanding of plasticity in these nuclei has limited the ability to test this hypothesis. Here, we used cDNA microarrays to monitor molecular correlates of plasticity induced by cerebellar learning paradigms which alter the vestibulo-ocular reflex (VOR). mRNAs were isolated selectively from the medial vestibular nucleus, the cerebellar target nucleus important for the VOR. Significant changes in transcript levels resulted from training paradigms that induced enduring increases or decreases in the gain of the VOR, but not from stimulus paradigms which delivered similar sensory inputs without inducing learning. The correlation between changes in VOR gain and gene transcription suggests a role for the medial vestibular nucleus in motor memory storage. Furthermore, a substantial number of transcripts that changed in specific association with learning showed oppositely directed changes in gene expression for increases and decreases in VOR gain. This points to a role for bi-directional modulation of signal transduction pathways in this form of motor learning. These experiments illustrate how applying microarrays to systems-level questions may help resolve the anatomical sites of plasticity and hasten the clarification of mechanistic relationships between different forms of learning.

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