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The role of m⁶A RNA methylation in maintaining cell type specific functions in the basal ganglia

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N⁶-methyladenosine (m⁶A) is the most abundant internal modification site in eukaryotic mRNA, affects almost every phase of mRNA metabolism and function. Although many studies have demonstrated the significant role of m⁶A methylation in neuron differentiation and brain development, the necessity of m⁶A methylation for maintaining normal neuronal functions in the adult brain has not been systematically studied yet. The striatum, as the input stage of the basal ganglia, has been long recognized as the key structure in mediating behaviors such as motivation, reward and learning. We generated adult mice carrying the conditional deletion of METTL14, an essential m⁶A methyltransferase complex, in D1 and D2 striatal neurons to study the role of m⁶A RNA methylation in maintaining cell type specific functions in the basal ganglia. We hypothesize that m⁶A deficiency will affect the normal neuronal activities of the striatal neurons, causing altered behavioral phenotypes. Through pharmacological approaches including selective agonist/antagonist and cocaine treatments, we found that *Mettl14* deletion disturbs the normal neuronal activities in D1 and D2 striatal neurons, leading to opposite behavioral phenotypes. By using in vivo fiber photometry recording, we found that *Mettl14* deletion causes a significant reduction in baseline firing activity and a weaker neuronal activity change induced by cocaine administration in the striatal neurons. Overall, our data indicate that m⁶A RNA methylation is significant in maintaining cell type specific neuronal functions and intrinsic cell excitabilities in the basal ganglia.