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CLIP-seq analysis of the RNA binding protein hnRNP H in striatum following methamphetamine administration in *Hnrnph1+/-* mice

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We recently mapped and validated *Hnrnph1* (heterogeneous nuclear ribonucleoprotein H1) as a quantitative trait gene for reduced methamphetamine (**MA**) behavioral sensitivity. Mice with heterozygous deletion of a small region in the first coding exon of *Hnrnph1* (*Hnrph1+/-*) showed reduced sensitivity to the stimulant, rewarding, reinforcing effect of MA as well as a decrease in MA-induced dopamine release relative to the wildtype. There is very little known about the mRNA targets in the brain or *in vivo* function of this RNA binding protein. Given that our data suggested a drug-induced cell biological mechanism by which *Hnrnph1* deletion affects MA neurobehavioral responding, we examined the change in hnRNP H RNA targets in response to MA. We optimized and performed cross-linking immunoprecipitation coupled with high-throughput sequencing (**CLIP-seq**) to understand hnRNP H-RNA interaction in the striatum (a brain region involved in addiction) of both wildtype and *Hnrnph1+/-* at baseline and in response to an acute dose of MA (2 mg/kg i.p.). Briefly, CLIP-seq involved the use of ultraviolet irradiation to generate covalent bond between RNA and proteins that are in close contact. Antibody specific to hnRNP H was then used to immunoprecipitate the protein-RNA complex followed by RNA extraction and reverse transcription of the extracted RNA into a cDNA library to be sequenced. This is the first CLIP-seq study to examine drug-induced changes in protein-RNA interactions in a specific functionally relevant brain region and will shed light on the molecular mechanism through which hnRNP H regulates methamphetamine-induced dopamine release and addictive behaviors.