Loss of KSRP allele increases spine density on prefrontal cortical pyramidal neurons

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The KH-type splicing regulatory protein (KSRP) is a multifunctional RNA-binding protein that has been implicated in variety of cellular processes including splicing, localization, and stability of neuronal mRNAs. More specifically, KSRP is an essential factor associated with the decay of AU-rich element (ARE)-containing mRNAs, which play important roles during nervous system development and regeneration. Previous studies indicated that loss of KSRP results in altered expression of Growth-Associated Protein 43 (GAP-43) and increased growth of hippocampal neurons in vitro (Bird et al., 2013). However, the effects of altered KSRP expression on neuronal function and brain development still remains to be elucidated. Here, we examined effect of altered KSRP expression on dendritic spine density and morphology on cortical neurons using Thy1-GFP mice crossed with both $KSRP^{-/-}$ and $KSRP^{+/-}$ vs $KSRP^{+/+}$ mice. We found that loss of KSRP alleles significantly increases spine density on layer V cortical pyramidal neuron in both $KSRP^{+/-}$ and $KSRP^{-/-}$ mice. Additionally loss of KSRP alleles increases growth of mossy fibers. By RT- ddPCR, neurites from cortical neurons cultured from these mice show increase in GAP-43 and CDC-42 mRNA levels in $KSRP^{+/-}$ and $KSRP^{-/-}$ neurites. Supporting these data, $KSRP^{-/-}$ mice show altered behavior in novel object recognition, trace fear conditioning and novelty induced hyperactivity. Together, these data indicate that KSRP impacts brain development and neuronal function that may be a reflection of altered subcellular levels of target mRNAs.