Rett syndrome (RTT) is a progressive neurodevelopmental disorder mainly caused by mutations in the X-linked *MECP2* gene. It affects 1 in 10.000 live female births and represents the main genetic cause of intellectual disability in girls worldwide. Besides neurons, astrocytes have been identified as active contributors to RTT pathogenesis as Mecp2 knock-out (KO) astrocytes fail to correctly support neuronal maturation and synaptogenesis. Indeed, culturing wild-type (WT) neurons with KO astrocytes or treating them with KO astrocyte-conditioned medium (ACM) affects their synaptic phenotype. Of note, one of the key synaptogenic factors released by astrocytes is cholesterol, which plays a crucial role in synapse formation and functioning. Several data highlight a defective cholesterol metabolism in RTT, supporting the hypothesis that abnormalities in astrocyte-produced cholesterol might contribute to synaptic dysfunctions. In this study, we report a downregulation of genes involved in cholesterol synthesis and secretion in primary KO astrocytes cultured alone or in co-culture with neurons and KO MACS-sorted astrocytes from P7 mice pups. Moreover, we demonstrate that cholesterol supplementation completely rescues synaptic defects not only in WT neurons treated with KO ACM but also in Mecp2 heterozygous (HET) neurons, which better recapitulate the genetic pattern of RTT patients.