Cytosine residues in DNA can be modified post-synthetically and this affects local protein-DNA interactions. For example, the MeCP2 protein specifically binds to methylated sites in the genome, potentially allowing it to interpret this epigenetic mark. Several clinical disorders are caused by mutations in the MECP2 gene, including the profound neurological disorder Rett syndrome. The equivalent phenotype in animal models can be reversed, suggesting that the protein fine-tunes neuronal function and that the human disorder may also be curable. Evidence will be presented that the root cause of Rett syndrome is failure of the primary function of MeCP2, which is to restrain gene expression in a DNA methylation-dependent manner.