

**Impact of Early Life Stress on Neural Network Dysregulation  
and Major Depressive Disorder in Adulthood**

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## **Abstract**

Early life stress (ELS) during childhood has been found to be directly associated with serious psychopathology in adults, which is often resistant to conventional treatment. There is growing evidence that ELS is linked to dysregulation of functional neural networks in adults. Specifically, previous studies of adults with ELS have demonstrated altered activation among the default mode network (DMN), executive control network (ECN), salience network (SN), and dorsal attention network (DAN), though findings have been inconsistent. The aim of the current study was to examine the relationship between retrospective self-reported ELS, including sexual, physical, and emotional abuse and neglect, and the extent and nature of impaired connectivity among functional neural networks using a resting-state fMRI paradigm with 35 adult outpatients diagnosed with major depressive disorder (MDD) and 20 non-depressed control participants. The degree of self-reported ELS was significantly higher in the MDD group than in controls. Furthermore, MDD was significantly associated with widespread hypo-connectivity between the DMN and DAN and the ECN and SN as well as hyper-connectivity within the DMN and DAN. Finally, ELS severity was associated with even greater hyper-connectivity within the DMN for MDD patients. This functional neural network dysregulation, potentiated by ELS, may play a critical role in producing the more pervasive and serious emotional lability, rumination, impaired self-reference, dysfunctional stress response, and obsessions and compulsions seen in MDD and related psychopathology. These findings suggest the importance of developing treatment methods that directly restore healthy balance to these critical functional neural networks impacted by childhood trauma.